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(54) **Cycloheptenopyridine derivatives, process for preparation thereof and antiulcer agents containing the same.**

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Description

This invention relates to cycloheptenopyridine derivatives useful as treatment agents for gastric or duodenal ulcer.

- 5 As for recent pathophysiological studies of gastric or duodenal ulcer, the behavior of potassium ion-dependent adenosine triphosphatase (hereinafter abbreviated as ($H^+ + K^+$) ATPase), which is involved in hydrochloric acid production in the gastric endoplasmic reticulum, vehicle has drawn attention, and the presence or absence of inhibitory activity of this enzyme has come to be used as an indicator for antiulcer agents (Gastroenterology vol. 1, 420, 1943 and ibid vol. 73, 921, 1977). It was revealed that this enzyme is located on parietal cells of the gastric mucosa and plays a role of a key enzyme of gastric proton pump, and blockade of this enzyme may be useful to suppress gastric acid secretion. At present, as typical examples of antiulcer agents which exhibit selective inhibitory action against this ($H^+ + K^+$) ATPase and are under development, there can be mentioned benzimidazole derivatives such as omeprazole having an unsubstituted or trisubstituted pyridylmethylsulfinyl group at the side chain (Japanese Laid-Open Patent Publication No. 141783/1979) and NC-1300 having an alkylaminophenylmethylsulfinyl group at the side chain (Japanese Laid-Open Patent Publication No. 60660/1986). Further, it has been known that some of the benzimidazole derivatives have a protecting activity for gastro-intestinal mucosal cell (Japanese Laid-Open Patent Publication No. 53406/1982).

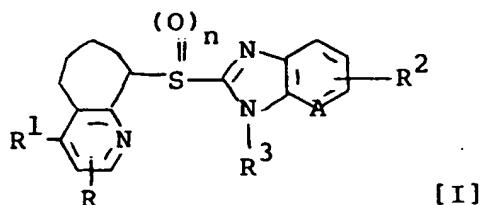
- 20 Histamine H_2 receptor antagonists represented by cimetidine exhibit excellent healing effect on peptic ulcer because they have a potent inhibitory action on gastric acid secretion. However, it is the present state of things that these drugs cannot simply be concluded to be satisfactory drugs because when administration thereof is discontinued due to complete healing, recurrence of ulcer is often observed, and that known ($H^+ + K^+$) ATPase inhibitors represented by omeprazole have a problem on stability and, therefore, their improvements are being desired. Further, peptic ulcers are generally thought to result from an imbalance 25 between the aggressive factors such as hydrochloric acid and pepsin and the defensive factors of the tunic mucosa side such as mucous secretion and mucosal bloodstream, and thus drugs having an inhibitory action on a gastric acid secretion and a cytoprotection together are being desired.

- 30 The present inventors vigorously studied to develop antiulcer agents which have a potent inhibitory action on gastric acid secretion and a cytoprotection together, and are physicochemically stable and further capable of being administered for treatment over a long period. As a result they have found cycloheptenopyridine derivatives having a potent inhibitory action on gastric acid secretion and a cytoprotection together.

Thus, according to this invention are provided cycloheptenopyridine derivatives represented by the general formula

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[wherin R represents a hydrogen atom or lower alkyl group; R¹ represents a hydrogen atom, halogen atom, lower alkoxy group, lower cycloalkoxy group, amido group, substituted phenoxy group, substituted benzyloxy group, lower alkoxy group optionally containing halogen atom(s), nitro group, hydroxyl group, lower alkenyloxy group, lower alkylthio group, or group-NR⁴R⁵ (wherein R⁴ and R⁵ may be the same or different and each represents a hydrogen atom or lower alkyl group, or R⁴ and R⁵ mutually combine together with the nitrogen atom adjacent thereto to form a 5- or 6- membered cycle); R² represents a hydrogen atom, halogen atom, lower alkyl group optionally containing a halogen atom, lower alkoxy group optionally containing a halogen atom, hydroxyl group, acyl group, lower alkoxy carbonyl group, nitro group or amino group; R³ represents a lower alkyl group, lower alkoxy methyl group, lower alkyl carbonyl group, lower alkoxy carbonyl group, carbamoyl group, lower alkyl carbamoyl group, lower alkyl carbonyl methyl group, lower alkoxy carbonyl methyl group, lower acyloxy methyl group, lower alkyl sulfonyl group, or physiologically acceptable protective group eliminable in an acid medium or under a physiological condition; n represents 0 or 1; and A represents a methine carbon or nitrogen atom] or their salts.

Cycloheptenopyridine derivatives represented by the general formula [I] include stereoisomers such as tautomers derived from the partial structure of benzimidazole, diastereomers derived from the partial structure of cycloheptenopyridine, enantiomers based on the asymmetric center, and the like.

Specific examples of R in the general formula [I] include, for example, a hydrogen atom, a lower alkyl group having 1 to 6 carbon atoms such as methyl, ethyl, propyl or butyl, etc.

Specific examples of R¹ in the general formula [I] include, for example, a hydrogen atom; a halogen atom such as a chlorine, bromine, iodine or fluorine atom; a lower alkoxy group having 1 to 6 carbon atoms such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, sec-butoxy, tert-butoxy or n-pentoxy; a lower alkenyloxy group such as allyloxy or butenyloxy; a lower alkoxy group substituted by halogen atom(s) such as 2,2,2-trifluoroethoxy or 2,2,3,3,3-pentafluoropropoxy; a lower alkoxy group substituted by a methoxy, ethoxy or n-propoxy group or the like; a lower alkoxy group substituted by a cyclopropoxy, cyclopropylmethoxy, cyclopentyloxy or cyclohexyloxy group or the like; a lower alkoxy group containing an aromatic ring such as phenoxy, tolyloxy, pyridyloxy or benzyloxy; a hydroxyl group; an amino group; a mono- or di-lower (C₁ to C₆) alkylamino group such as methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, n-propylamino, n-butylamino or tert-butylamino; a cyclic amino group to form a 5- or 6-membered ring such as pyrrolidino, piperidino, morpholino, piperazino, N-methylpiperazino or the like; etc.

Specific examples of R² in the general formula [I] include, for example, a hydrogen atom; a halogen atom such as a chlorine, bromine, iodine or fluorine atom; a lower alkyl group having 1 to 6 carbon atoms such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl or tert-butyl; a lower alkoxy group having 1 to 6 carbon atoms such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, sec-butoxy, tert-butoxy or n-pentoxy; a lower alkyl or lower alkoxy group substituted by halogen atom(s) such as trifluoromethyl, 2-fluoroethyl, difluoromethyl, 2,2,2-trifluoroethoxy or 2,2,3,3,3-pentafluoropropoxy; a hydroxyl group; an acyl group having 1 to 6 carbon atoms such as acetyl, propionyl or butyryl; an aryl group such as benzoyl; a lower alkoxy carbonyl group having 1 to 6 carbon atoms such as methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, isopropoxycarbonyl, n-butoxycarbonyl, sec-butoxycarbonyl, tert-butoxycarbonyl or n-pentoxy carbonyl; a nitro group; an amino group (including a lower alkylamino group); etc.

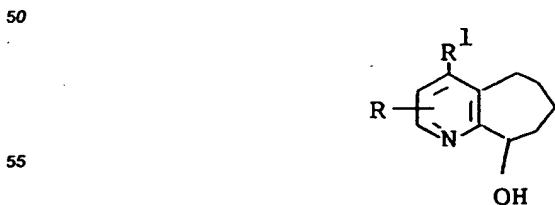
Specific examples of R³ in the general formula [I] include, for example, a hydrogen atom; a lower alkyl group having 1 to 6 carbon atoms such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl or tert-butyl; a lower alkoxy methyl group such as methoxymethyl, ethoxymethyl or propoxymethyl; an acyl group having 1 to 6 carbon atoms such as acetyl, propionyl or butyryl; an aryl group such as benzoyl; an acyloxymethyl group having 1 to 6 carbon atoms such as acetoxy methyl, propionyloxymethyl or butyryloxymethyl; an aroyloxymethyl group such as benzoyloxymethyl or toluyloxymethyl; a lower alkoxy carbonyl group having 1 to 6 carbon atoms such as methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, isopropoxycarbonyl, n-butoxycarbonyl, sec-butoxycarbonyl, tert-butoxycarbonyl or n-pentoxy carbonyl; a carbamoyl group, or a carbamoyl group substituted by a lower alkyl group having 1 to 6 carbon atoms such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl or tert-butyl; a lower alkylsulfonyl group having 1 to 6 carbon atoms whose lower alkyl moiety is exemplified by methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl or the like; etc.

As salts of the compounds of the invention are mentioned pharmacologically acceptable addition salts with suitable alkali metal ions. Mentioned for example are salts with sodium, potassium, calcium, magnesium, etc.

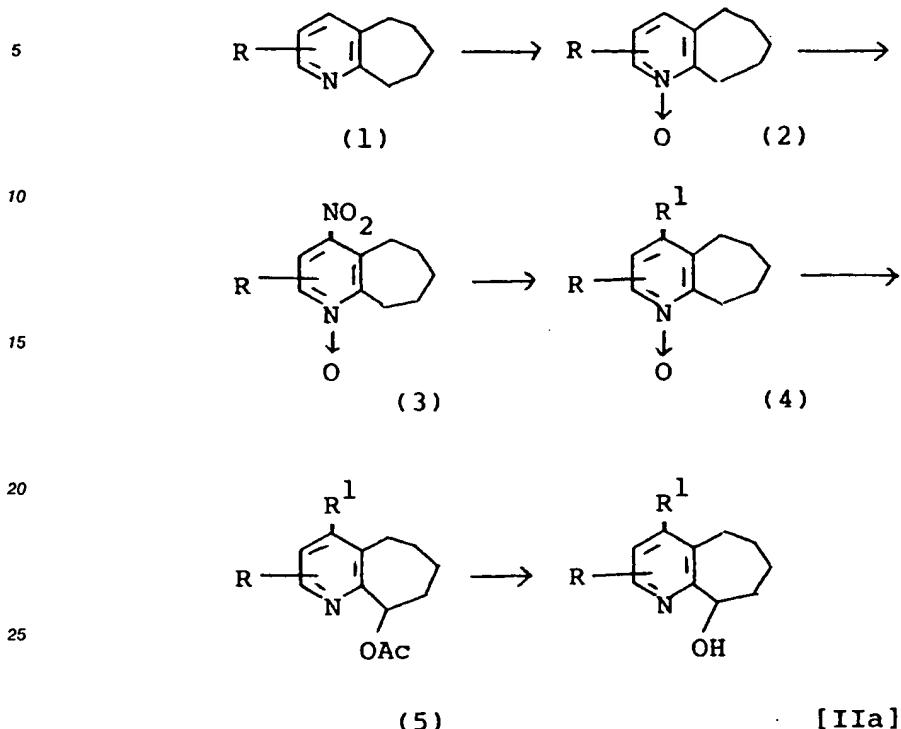
Compounds [I] are mainly characterized by having a cycloheptenopyridine ring, and formation and introduction of this cycloheptenopyridine ring as well as formation and introduction of the benzimidazole ring and imidazopyridine ring can be carried out according to any pertinent synthetic method.

(a) Formation of the cycloheptenopyridine ring

Some of 9-hydroxy-2,3-cycloheptenopyridine derivatives having a cycloheptenopyridine ring and represented by the formula [IIa]



(wherein R and R¹ are as defined above) are novel substances, and can be synthesized by the synthetic route shown below.



Namely a compound [IIa] can be synthesized by subjecting to a known oxidation reaction of a substituted or unsubstituted 2,3-cycloheptenopyridine derivative (1) either commercially available or synthesized according to a method disclosed in the literatures [Yakugaku Zasshi (Journal of Pharmacology) 78 268 (1975); J. AM. CHEM. SOC., 79 402 (1957); J.C.S., Perkin Transl 1973 (9) 968.], nitrating the resulting 2,3-cycloheptenopyridine derivative (2), subjecting the resulting nitrated compound to substitution reaction(s) to form the corresponding 4-substituted-2,3-cycloheptenopyridine-N-oxide derivative (4), rearranging the compound (4) with heating in the presence of acetic anhydride, and hydrolyzing the resulting compound with an alkali.

Preparation of the compound (3) from the compound (2) can be carried out by directly nucleophilic substitution of the compound (2). Further, an alkoxy derivative or amine derivative can be obtained by once converting a compound (2) to the corresponding 4-halo-2,3-cycloheptenopyridine-N-oxide derivative and then reacting the 4-halo derivative, for example in the presence of a base, either with an alcohol such as methanol, ethanol, propanol, allyl alcohol, 2,2,2-trifluoroethanol, 2,2,3,3-tetrafluoropropanol, benzyl alcohol or methoxyethyl alcohol, or with ammonia or an amine such as methylamine, ethylamine, dimethylamine, piperazine, piperidine, pyrrolidine or N-methylpiperazine.

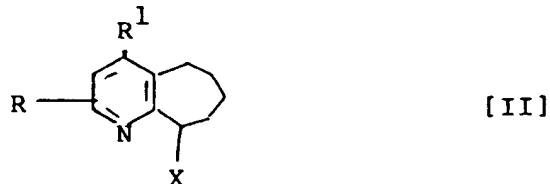
This reaction can be carried out in the presence of a base at an appropriate temperature of ice-cooling to boiling point of the solvent either using a nucleophilic reagent itself represented by R¹ as a solvent or using an organic solvent such as tetrahydrofuran, dioxane, acetone, acetonitrile, N,N-dimethylformamide or hexamethyl phosphoric triamide. When an amine derivative is obtained, the reaction is carried out, preferably in a sealed tube, for about 1 to 48 hours. Examples of bases used in this reaction include alkali metals such as sodium, potassium and lithium; alkali metal hydrides such as sodium hydride and potassium hydride; alcoholates such as potassium t-butylate and sodium methylate; alkali metal hydroxides such as lithium hydroxide, sodium hydroxide and potassium hydroxide; and alkali metal carbonates such as sodium hydrogen carbonate and potassium hydrogen carbonate. The resulting compound (4) is heated (80 to 150 °C) in the presence of acetic anhydride alone or sulfuric acid or perchloric acid or the like to give the corresponding 9-acetoxy-2,3-cycloheptenopyridine derivative (5), which is then hydrolyzed in the presence of a base, for example, an alkali metal hydroxide such as sodium hydroxide or potassium hydroxide, or an alkali metal carbonate such as sodium hydrogen carbonate or potassium carbonate, whereby the

corresponding compound [IIa] can be prepared. Examples of the solvent used include methanol, ethanol, water, etc. The reaction is usually completed in 10 minutes to 2 hours at a temperature of room tempeature to the boiling point of the solvent.

5 (b) Synthesis of compounds [I]

Compounds of the formula [I] can be synthesized according to various methods. For example, a reactive derivative represented by the general formula

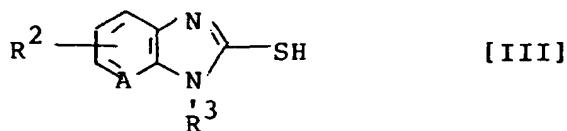
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(wherein X represents a halogen atom, or an alkylsulfonyl or arylsulfonyl group, and R and R¹ are as defined above) is reacted with a 2-mercaptopbenzimidazole or 2-mercaptop[4,5-b]imidazopyridine derivative represented by the general formula

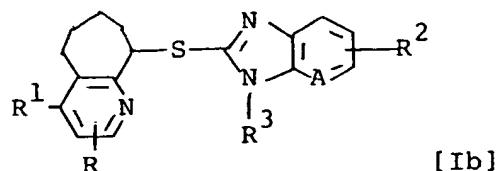
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(wherein R², R³ and A are as defined above) or a salt thereof to prepare a sulfide type compound [Ib] where n in the general formula [I] expresses zero.

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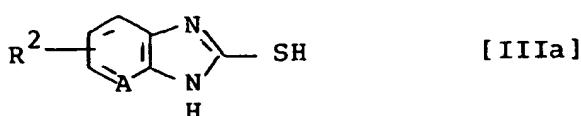
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A reactive derivative [II] can be obtained either by reacting a compound [IIa] with a halide such as thionyl chloride, phosphorus oxychloride, phosphorus trichloride, phosphorus tribromide, p-toluenesulfonyl chloride or the like, or by reacting an aforementioned compound (4) with a halogenating reagent such as thionyl chloride, phosphorus oxychloride, phosphorus trichloride, p-toluenesulfonyl chloride or 1,3,5-trichlorocyanuric acid.

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A sulfide type compound [Ib] can also be obtained by reacting a reactive derivative [II] with a 2-mercaptopbenzimidazole derivative or 2-mercaptop[4,5-b]imidazopyridine derivative represented by the general formula

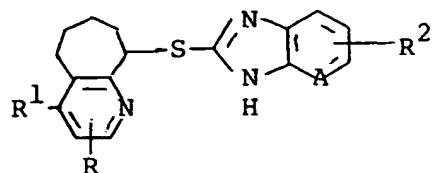
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(wherein R² and A are as defined above) or a salt thereof to obtain a compound of the general formula

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[Ia]

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, and then, if desired, subjecting the compound [Ia] to a known N-alkylation reaction, N-acylation reaction or N-sulfonylation reaction.

Specific examples of X in the reactive derivative [II] include, for example, halogen atoms such as 15 chlorine, bromine and iodine atoms; lower alkylsulfonyloxy groups such as methanesulfonyloxy and ethanesulfonyloxy; arylsulfonyloxy groups such as benzenesulfonyloxy and p-toluenesulfonyloxy; etc. Examples of the salts of the compounds [III] and [IIIa] include salts with alkali metals such as sodium and potassium.

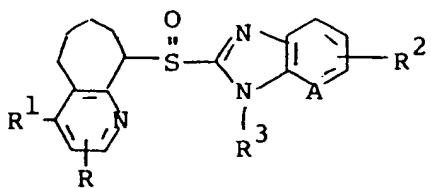
The reaction to condense a reactive derivative [II] with a compound [III] or [IIIa] is preferably carried out 20 in a hydrophilic organic solvent such as methanol, ethanol, acetone, tetrahydrofuran, N,N-di-methylformamide or dimethylsulfoxide or in a mixed solvent of such a solvent and water. The reaction temperature is in the range of 0 to 150 °C, preferably 80 to 100 °C, and it is preferred that the reaction is carried out in the presence of a base.

Examples of the base include alkali metal hydroxides such as sodium hydroxide and potassium 25 hydroxide; alkali metal carbonates such as sodium carbonate, potassium carbonate, sodium hydrogen carbonate and potassium hydrogen carbonate; organic amines such as triethylamine, pyridine and N,N-dimethylaniline; etc. The reaction is usually completed in 3 to 12 hours.

After completion of the reaction, the reaction solution is subjected to conventional methods, for example, usually adopted means such as extraction, recrystallization and chromatography to obtain the 30 compound [Ia] or [Ib].

Further, a sulfoxide type compound [Ic] which corresponds to a compound of the general formula [I] wherein n is 1 can be prepared by oxidizing a compound [Ia] or [Ib] or a salt thereof.

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[Ic]

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The oxidation reaction of a compound [Ia] or [Ib] can be carried out in benzene, chloroform, methylene chloride, methyl acetate, ethyl acetate, acetonitrile, methanol, N,N-dimethylformamide, N,N-dimethylacetamide, acetic acid, formic acid, water or another solvent or a mixed solvent thereof using an equivalent amount of an oxidizing agent. Usually, the reaction is carried out at -30 °C to room temperature 45 and completed in 5 minutes to 2 hours. As examples of the oxidizing agent are mentioned oxidizing agents usually used for oxidation of sulfides such as peracetic acid, hydrogen peroxide, trifluoroperacetic acid, m-chloroperacetic acid and sodium metaperiodate. After completion of the reaction the compound [Ic] can be obtained from the reaction solution by conventional methods, for example, by usual separation and purification means such as extraction, recrystallization and chromatography.

The inhibitory action on gastric acid secretion and cytoprotection of the following compounds, which are representative examples of compounds [I] of the invention, are detailedly described below:

55 63), 9-(5-Methoxybenzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine (compound of Example

68), 9-(Benzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine sodium salt (compound of Example

75), 9-(5-Methylbenzimidazole-2-yl)sulfinyl-2,3-cycloheptenopyridine (compound of Example 75).

9-(Benzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine (compound of Example 77),
 9-(5-Fluorobenzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine (compound of Example 78),
 9-(Benzimidazole-2-yl)sulfinyl-4-(2-methoxyethoxy)-2,3-cycloheptenopyridine (compound of Example
 96), and
 5 9-(Benzimidazole-2-yl)sulfinyl-4-methoxy-3-methyl-2,3-cycloheptenopyridine (compound of Example
 109)

(a) Inhibitory effect on gastric acid secretion in Ghosh-Schild rats

10 Each of male Wistar-KV rats was fasted for 24 hours, and a trachea cannula was set up under urethane anesthesia. The abdomen was incised, a double cannula was set up at the forestomach, and then the abdomen was closed. The gastric acid secretion was stimulated by intravenous infusion of 10 µg/kg/hr. Physiological saline was perfused into the stomach through the double cannula at a rate of 1 ml/min., and the effluent was collected every 10 minutes. The acidity of the effluent was measured, using an automatic titrator, by titrating the effluent with 1/100 N sodium hydroxide to pH 7. When the acid secretion had reached a stable plateau, the test drug was intravenously administered, and the gastric acid secretion was measured 3 hours after the test drug administration. The antisecretory effect was expressed as percentages to the secretory amount before administration of the test compound. The results are shown in Table-1.

20 (b) Inhibitory effect on formation of gastric lesion induced by ethanol

Male Wistar rats weighing 170 to 270 g were used. Each rats was placed in the separate cages to deprive of food but allowed free access to water for 4 hours. Test drugs or the control drug were orally administered respectively in amounts of 3, 10 and 30 mg/kg, and 30 minutes thereafter 1 ml of 99.5 % ethanol were orally administered respectively. One hour after the ethanol administration the rats were sacrificed by cervical vertebrae dislocation, and the stomachs were removed with 8 ml of 1 % formalin and put into 1 % formalin for 30 minutes to fix the gastric wall. After the fixing, each stomach was opened along the greater curvature, and then after the mucosal surface was washed with tap water, the total length lesions generated at the glandular portion was determined as an ulcer index.

30 The antiulcer effect by the test drug was expressed by the ED₅₀ value (the dose of the test compound to inhibit the ulcer by 50 % to the ulcer index of the non-treated group). The results are shown in Table-2. Only the solvent was administered to the non-treated group.

Table 1

Example No.	Inhibiting action of gastric acid secretion (rat i.v.)	
	3 mg/kg	1 mg/kg
63	73.8 %	45.7 %
68	-	54.9 %
75	42.1 %	-
77	74.7 %	44.7 %
78	82.9 %	65.4 %
96	57.4 %	38.6 %
45 109	77.6 %	-
Omeprazole (Control drug)	-	36.9 %

Inhibition percentages at 180 minutes after the administrations are shown.

Table 2

Example No.	ED ₅₀ value (mg/kg P.O.)
77	13.0
68	10.9

As apparent from the above test results, compounds [I] are potent treatment drugs for gastric or duodenal ulcer.

An antiulcer agent containing as an active ingredient a compound of the formula [I] or a salt thereof can mainly be orally or parenterally administered (for example, administered by intramuscular injection, 5 intravenous injection, subcutaneous administration, rectal administration, transcutaneous administration, or the like), and preferably be orally administered, and various drug forms suitable for the respective administrations can be adopted. As for solid formulations, a compound [I] can be formulated into tablets, capsules, granules, powders or fine granules, and can also be formulated in enteric coated agents by a coating technique therefor. Further, a liquid agent can be prepared by converting a compound [I] to an alkali 10 salt or physiologically acceptable salt, and then dissolving the salt in water or an aqueous alkali solution.

Although the dose of a compound [I] to patients is varied depending on the age, the condition of the disease and the like, it is generally preferred to administer it to an adult in an amount of 0.5 to 1,000 mg, particularly 1 to 200 mg, divided into 1 to 3 times, per day.

Syntheses of starting compounds used in the invention and compounds [I] of the invention are more 15 specifically and detailedly described below according to reference examples and examples, but the invention should not be limited thereto.

Reference example 1

20 2,3-Cycloheptenopyridine-N-oxide

1) 14.72 g (0.1 mol) of 2,3-Cycloheptenopyridine is dissolved in 150 ml of dichloromethane, 21.57 g (0.1 mol) of m-chloroperbezoic acid is added by portions under ice cooling and stirring, and the mixture is stirred at the same temperature for 3 hours. After the reaction, 150 ml of a saturated aqueous sodium 25 hydrogen carbonate solution is added, followed by extraction with methylene chloride. The methylene chloride layer is sufficiently washed with a saturated aqueous sodium hydrogen carbonate solution and saturated saline, and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting solid residue is recrystallized from ether-n-hexane to obtain 14.13 g (86.6 %) of 2,3-cycloheptenopyridine-N-oxide as grayish white crystals having a melting point of 107 to 30 109 °C.

IR_vmax(KBr): 3080, 2924, 1610, 1432, 1268, 1246, 810 cm⁻¹.

NMR(CDCl₃)δ: 1.09-2.03(6H,m), 2.57-2.91 (2H,m), 3.18-3.50(2H,m), 6.68-7.03(2H,m), 7.92-8.23(1H,m).

2) 14.72 g (0.1 mol) of 2,3-cycloheptenopyridine is dissolved in 100 ml of acetic acid, and 13.3 ml of 30 % aqueous hydrogen oxide is added, followed by 8 hour stirring with heating at 100 °C. 7.4 ml of 30 % Aqueous hydrogen oxide is further added, and then after 8 hour stirring with heating, the solvent is 35 distilled away under reduced pressure. The resulting residue is extracted with chloroform, and the extract is sufficiently washed with a saturated aqueous sodium hydrogen carbonate solution and saturated saline and dried over anhydrous magnesium sulfate. Then, the solvent is distilled away under reduced pressure 40 to obtain almost quantitatively 2,3-cycloheptenopyridine-N-oxide.

Reference example 2

4-Nitro-2,3-cycloheptenopyridine-N-oxide

45 3.92 g (24 mmoles) of 2,3-cycloheptenopyridine-N-oxide is dissolved in 15 ml of sulfuric acid under ice cooling, and the solution is stirred for 40 minutes with heating at 85 to 90 °C, while 13 ml of fuming nitric acid is added dropwise thereto. After the reaction, ice water is added, and after neutralization with a 40 % aqueous sodium hydroxide solution, the mixture is extracted with methylene chloride. The methylene 50 chloride layer is washed with saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure to obtain 2.23 g (44.6 %) of 4-nitro-2,3-cycloheptenopyridine-N-oxide as yellowish crystals having a melting point of 118 to 120 °C.

IR_vmax(KBr): 3110, 2928, 2852, 1529, 1570, 1516, 1422, 1340, 1272, 1144, 828, 700 cm⁻¹.

NMR(CDCl₃)δ: 1.54-2.08(6H,m), 2.85-3.17 (2H,m), 3.27-3.63(2H,m), 7.46 (1H,d,J=8Hz), 8.11-55 (1H,d,J=8Hz).

Reference example 3**4-chloro-2,3-cycloheptenopyridine-N-oxide**

5 2.23 g (10.7 mmol) of 4-Nitro-2,3-cycloheptenopyridine-N-oxide is added by portions to 7.85 g (0.1 mol) of acetyl chloride under ice cooling and stirring, and the mixture is stirred at the same temperature for 1 hour. After the reaction, the mixture is poured into ice water, followed by extraction with ethyl acetate. The ethyl acetate layer is washed with saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is purified by silica gel column chromatography (chloroform-methanol 95:5) and recrystallized from ether-n-hexane to obtain 1.77 g (83.9 %) of 4-chloro-2,3-cycloheptenopyridine-N-oxide as yellowish prismatic crystals having a melting point of 117 to 118 °C.

IR_vmax(KBr): 3112, 2924, 2848, 1438, 1418, 1336, 1256, 1170, 1110, 830, 710 cm⁻¹.

10 NMR(CDCl₃)δ: 1.50-2.05(6H,m), 2.80-3.15 (2H,m), 3.22-3.55(2H,m), 7.03 (1H,d,J=8Hz), 7.99-15 (2H,d,J = 8Hz).

Reference example 4**4-Methoxy-2,3-cycloheptenopyridine-N-oxide**

20 810 mg (3.89 mmol) of 4-nitro-2,3-cycloheptenopyridine-N-oxide is dissolved in 10 ml of methanol, 250 mg of sodium hydroxide is added thereto, and the mixture is refluxed for 45 minutes. After cooling, the methanol is distilled away under reduced pressure, the resulting residue is extracted with chloroform. The chloroform layer is washed with saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is purified by silica gel column chromatography (chloroform-methanol 95:5) and recrystallized from ethyl acetate to obtain 710 mg (94.5 %) of 4-methoxy-2,3-cycloheptenopyridine-N-oxide as yellowish prismatic crystals having a melting point of 148 to 149 °C.

IR_vmax(KBr): 3075, 2916, 2848, 1615, 1570, 1460, 1428, 1344, 1284, 1242, 1188, 1034, 828, 746 cm⁻¹.

30 NMR(CDCl₃)δ: 1.43-2.04(6H,m), 2.65-2.97(2H,m), 3.20-3.54(2H,m), 3.83(3H,s), 6.57(1H,d,J=8Hz), 8.08-(1H,d,J = 8Hz).

Reference example 5**4-(3-Methoxypropoxy)-2,3-cycloheptenopyridine-N-oxide**

35 1.28 g (14.2 mmol) of 1-methoxypropanol is dissolved in 7 ml of dimethylsulfoxide (DMSO) in an argon stream, 566 mg (14.2 mmol) of 60 % sodium hydride is added thereto, and the mixture is stirred at 60 °C for 30 minutes. Under stirring at room temperature, 1.40 g (7.08 mmol) of 4-chloro-2,3-cycloheptenopyridine-N-oxide dissolved in 5 ml of DMSO is added dropwise, followed by stirring at 40 °C for 1 hour. Thereafter, with stirring at room temperature, 566 mg (14.2 mmol) of 60 % sodium hydride and 310 mg (3.44 mmol) of 1-methoxypropanol are added, and the mixture is stirred at 40 °C for 16 hours. After cooling, the reaction mixture is poured in ice-saline, followed by extraction with chloroform. The chloroform layer is washed with saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is purified by silica gel column chromatography (chloroform-methanol 40:1) to obtain 1.15 g (64.5 %) of 4-(3-methoxypropoxy)-2,3-cycloheptenopyridine-N-oxide as a palely brown oily substance.

IR_vmax(Neat): 2928, 2856, 1450, 1342, 1288, 1240, 1200, 1188, 1136, 1120, 1092, 1064, 1028, 750, 662 cm⁻¹.

50 NMR(CDCl₃)δ: 1.40-2.00(6H,m), 2.04(2H,t, J=6Hz), 2.63-2.94(2H,m), 3.31 (3H,s), 3.20-3.65(4H,m), 4.04 (2H,t,J = 7Hz), 6.57(1H,d,J = 7Hz), 8.03(1H,d,J = 7Hz).

Reference example 6**4-(2-benzyloxyethoxy)-2,3-cycloheptenopyridine-N-oxide**

In a stream of argon, 804 mg (20.1 mmol) of 60 % sodium hydride is suspended in 7 ml of DMSO, 2.86 ml (20.1 mmol) of 2-benzyloxyethanol is added dropwise with stirring at room temperature, and the mixture

is stirred at 60 °C for 35 minutes. Further, 1.40 g (7.05 mmol) of 4-chloro-2,3-cycloheptenopyridine-N-oxide dissolved in 5 ml of DMSO is added dropwise thereto with stirring at room temperature, and the mixture is stirred at 40 °C for 3 hours and 20 minutes. After cooling, the reaction mixture is poured in ice water, followed by extraction with methylene chloride. The methylene chloride layer is washed successively with
 5 water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is purified by silica gel column chromatography (chloroform-methanol 40:1) to obtain 2.12 g (96.1 %) of 4-(2-benzyloxyethoxy)-2,3-cycloheptenopyridine-N-oxide as a palely brown oily substance.

IR_vmax(Neat): 2924, 2852, 1444, 1342, 1290, 1242, 1200, 1166, 1134, 1092, 1068, 1034, 892, 758, 744,

10 690 cm⁻¹.

NMR(CDCl₃)δ: 1.43-2.05(6H,m), 2.70-3.00 (2H,m), 3.25-3.55(2H,m), 3.70-3.96(2H,m), 4.00-4.24(2H,m),
 4.60(2H,s), 6.58(1H,d,J=8Hz), 7.30(5H,bs), 8.04(1H,d,J=8Hz).

Reference example 7

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4-(2-Hydroxyethoxy)-2,3-cycloheptenopyridine-N-oxide

In a stream of argon, 1.63 g (70.0 milligram atoms) of metal sodium is added by portions to 28 ml of ethylene glycol under ice cooling and stirring, and the mixture is stirred for 1 hour with heating at 100 °C.

20 Then, 7.00 g (35.0 mmol) of 4-chloro-2,3-cycloheptenopyridine-N-oxide is added with stirring at room tempeature, and the mixture is stirred at 120 °C for 3 hours and 30 minutes. After the reaction, the mixture is poured in ice water, followed by extraction with chloroform. The chloroform layer is dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is crystallized from ethanol-ether to give 3.09 g (38.9 %) of 4-(2-hydroxyethoxy)-2,3-cycloheptenopyridine-N-oxide as colorless pillar crystals having a melting point of 159-160 °C. The mother liquor is concentrated,
 25 and the residue is purified by silica gel column chromatography (chloroform-methanol 20:1 → 15:1 → 10:1) to give 2.62 g (33.4 %) of the desired substance (total yield 72.3 %).

IR_vmax(KBr): 3224, 3104, 2912, 2852, 1450, 1344, 1292, 1236, 1204, 1186, 1138, 1092, 1062, 1032, 890, 822, 758 cm⁻¹.

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NMR(CDCl₃)δ: 1.35-2.10(6H,m), 2.65-3.03(2H,m), 3.22-3.55(2H,m), 3.55- 4.15(5H,m), 6.57(1H,d,-J=7Hz), 7.97(1H,d,J=7Hz).

Reference example 8

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4-(2-Chloroethoxy)-2,3-cycloheptenopyridine-N-oxide

In a stream of argon, 2.23 g (10.0 mmol) of 4-(2-hydroxyethoxy)-2,3-cycloheptenopyridine-N-oxide is dissolved in 22 ml of chloroform, 1.97 ml (27.0 mmol) of thionyl chloride is added dropwise thereto with stirring at -12 °C, and the mixture is stirred at room temperature for hours and 20 minutes and then stirred
 40 at 60 °C for 1 hour and 15 minutes. After cooling, the reaction mixture is poured into ice - a saturated aqueous sodium hydrogen carbonate solution, followed by extraction with chloroform. The chloroform layer is washed successively with a saturated aqueous sodium hydrogen carbonate solution and water and dried over anhydrous magnesium sulfate, and then the solvent is distilled away under reduced pressure. The resulting residue is purified by silica gel column chromatography (chloroform-methanol 20:1) to give 2.15 g
 45 (89.1 %) of 4-(2-chloroethoxy)-2,3-cycloheptenopyridine-N-oxide as colorless needle crystals having a melting point of 109 to 110.5 °C.

IR_vmax(KBr): 2924 2852, 1448, 1292, 1240, 1200, 1190, 1068, 1032, 824, 814, 774 cm⁻¹.

NMR(CDCl₃)δ: 1.39-2.01(6H,m), 2.66-3.00 (2H,m), 3.20-3.53(2H,m), 3.80 (2H,t,J=6Hz), 6.55(1H,d,J=8Hz), 8.05(1H,d,J=8Hz).

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Reference example 9

4-[2-(2-pyridylmethoxy)ethoxy]-2,3-cycloheptenopyridine-N-oxide

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In a stream of argon, 2.23 g (10.0 mmol) of 4-(2-hydroxyethoxy)-2,3-cycloheptenopyridine-N-oxide is suspended in 30 ml of tetrahydrofuran (THF), 600 mg (15.0 mmol) of 60 % sodium hydride is added by portions thereto under ice cooling and stirring, and the mixture is stirred at room temperature for 10 minutes. Then, after 20 minutes stirring at 50 °C, 1.65 g (12.90 mmol) of picolyl chloride dissolved in 15 ml

of THF is added dropwise thereto with stirring at room temperature, and the mixture is stirred at 90 °C for 8 hours. Then, after 12 hours stirring at room temperature, 200 mg (5 mmol) of 60 % sodium hydride is added, and the mixture is refluxed with heating for 3 hours. After the reaction, the solvent is distilled away under reduced pressure, the residue is added to ice water, and the mixture is extracted with methylene chloride. The methylene chloride layer is dried over anhydrous magnesium sulfate, and the solvent distilled away under reduced pressure. The resulting residue is purified by silica gel column chromatography (chloroform-methanol 30:1 → 10:1) to give 2.33 g (74.2 %) of 4-[2-(2-pyridylmethoxy)ethoxy]-2,3-cycloheptenopyridine-N-oxide as a brown oily substance.

IR_vmax(Neat): 2924 2852, 1590, 1446, 1342, 1290, 1240, 1200, 1134, 1092, 1064, 1036, 892, 758 cm⁻¹.
 NMR(CDCl₃)δ: 1.37-2.02(6H,m), 2.70-3.02 (2H,m), 3.21-3.51(2H,m), 3.80-4.03(2H,m), 4.05-4.31(2H,m), 6.59(1H,d,J = 8Hz), 7.03-7.78 (3H,m), 8.04(1H,d,J = 8Hz), 8.51 (1H,d,J = 8Hz).

Reference example 10

15 4-[2-(2-oxopyrrolidin-1-yl)ethoxy]-2,3-cycloheptenopyridine-N-oxide

In a stream of argon, 632 mg (15.8 mmol) of 60 % sodium hydride is suspended in 30 ml of dimethylformamide (DMF), 1.12 g (13.1 mmol) of 2-pyrrolidone is added thereto under ice cooling, and the mixture is stirred at 80 °C for 1 hour and 30 minutes. Then, under stirring at room temperature, 2.11 g (8.73 mmol) of 4-(2-chloroethoxy)-2,3-cycloheptenopyridine-N-oxide dissolved in 15 ml of DMF is added dropwise, and the mixture is stirred at 60 °C for 2 hours and 10 minutes. After cooling the mixture is poured into a saturated aqueous sodium hydrogen carbonate solution, followed by extraction with methylene chloride. The methylene chloride layer is dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is subjected to separation and purification by silica gel column chromatography (chloroform-methanol 20:1 → 10:1 → 4:1) to obtain 334 mg (53.3 %) of 4-[2-(2-oxopyrrolidin-1-yl)ethoxy]-2,3-cycloheptenopyridine-N-oxide as colorless powder having a melting point of 112 to 115 °C.

IR_vmax(KBr): 2924, 1672, 1452, 1344, 1292, 1240, 1202, 1188, 1138, 1092, 1068, 1028, 886, 832, 758 cm⁻¹.
 NMR(CDCl₃)δ: 1.40-2.56(10H,m), 2.65-3.00 (2H,m), 3.25-3.62(4H,m), 3.68 (2H,t,J = 6Hz), 4.09-4.12(2H,t,J = 6Hz), 6.55(1H,d,J = 8Hz), 8.04(1H,d,J = 8Hz).

Reference example 11

35 4-Ethoxy-3-methyl-2,3-cycloheptenopyridine-N-oxide

1.00 g (4.50 mmol) of 4-nitro-3-methyl-2,3-cycloheptenopyridine-N-oxide is dissolved in 15 ml of ethanol, 540 mg (13.5 mmol) of sodium hydroxide is added thereto under ice cooling and stirring, and after stirring at room temperature for 19 hours, the mixture is refluxed with heating for 30 minutes. After cooling, the ethanol is distilled away under reduced pressure and the resulting residue is extracted with chloroform. The chloroform layer is washed successively with water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is purified by silica gel column chromatography (chloroform-methanol 40:1) to obtain 679 mg (68.2 %) of 4-ethoxy-3-methyl-2,3-cycloheptenopyridine-N-oxide as palely brown powder having a melting point of 107 to 108 °C.

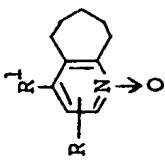
IR_vmax(KBr): 2976, 2932, 2852, 1478, 1454, 1420, 1388, 1332, 1248, 1228, 1192, 1168, 1136, 1052, 1026, 966, 928, 868 cm⁻¹.
 NMR(CDCl₃)δ: 1.42(3H,t,J = 7Hz), 1.50-2.03 (6H,m), 2.16(3H,s), 2.65-3.93 (2H,m), 3.23-3.48(2H,m), 3.81 (2H,q,J = 7Hz), 7.95(1H,s).

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Compounds shown in Table-3 are obtained in the same manner as Reference examples 1 to 11.

Table-3 (1)



Reference Example No.	R	R ¹	Melting point (yield)	IR cm ⁻¹	NMR (CDCl ₃) δ
12	H	OCH ₂ CH ₂ OCH ₃	Palely brown pillar crystal (56.0 %) 71-73 °C	[KBr] 3016, 2980, 2920, 2872, 2852, 1454, 1292, 1240, 1190, 1136, 1120, 1092, 1064, 1034, 760,	1.41-2.00 (6H,m), 2.66-3.03 (2H,b,J=10Hz), 3.41 (5H,bs), 3.58-3.86 (2H,m), 3.95-4.30 (2H,m), 6.57 (1H,d,J=8Hz), 8.03 (1H,d,J=8Hz)
13	H	OCH ₂ CH ₂ =CH ₂	Colorless amorphous powder (50.9 %)	[KBr] 2916, 1448, 1422, 1344, 1292, 1238, 1204, 1188, 1138, 1062, 1028, 1000, 924, 884, 826, 810, 766, 744, 149-150 °C	1.40-2.03 (6H,m), 2.70-3.03 (2H,m), 3.20-3.55 (2H,m), 4.52 (2H,d,J=5Hz), 5.10-5.58 (2H,m), 5.76-6.23 (1H,m), 6.56 (1H,d,J=7Hz), 8.03 (1H,d,J=7Hz)
14	H	OCH ₂ C≡C ₃	Colorless needle crystal (48.6 %) 166-169 °C	[KBr] 2920, 2944, 1454, 1296, 1274, 1240, 1202, 1174, 1160, 1134, 1098, 1038, 972, 862, 764,	1.40-2.17 (6H,m), 2.60-3.04 (2H,m), 3.16-3.56 (2H,q,J=8Hz, 16Hz), 6.55 (1H,d,J=8Hz), 8.07 (1H,d,J=8Hz)
15	H	OCH ₂ CF ₂ CF ₃	Colorless prismatic crystal (72.8%) 135-138 °C	[KBr] 2940, 1454, 1346, 1298, 1272, 1240, 1216, 1188, 1136, 1110, 1094, 1068, 1040, 1026, 956, 810, 764,	1.45-2.05 (6H,m), 2.70-2.97 (2H,m), 3.25-3.50 (2H,t,J=12Hz), 6.55 (1H,d,J=5Hz), 8.08 (1H,d,J=5Hz)
16	H	OCH ₂ CF ₂ CF ₃	Colorless powder (60.0%) 106.5-108 °C	[KBr] 2936, 1478, 1452, 1346, 1296, 1270, 1240, 1200, 1136, 1098, 1068, 1036, 962, 950, 886, 840, 832, 810, 768,	1.45-2.05 (6H,m), 2.68-2.95 (2H,m), 3.25-3.50 (2H,m), 4.35 (2H,t,J=12Hz), 5.36, 5.96, 6.52 (1H,tx3,J=3Hz), 6.57 (1H,d,J=6Hz), 8.07 (1H,d,J=6Hz)

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Table-3 (2)

Reference Example No.	R	R ¹	Melting point (yield)	IR[cm ⁻¹]	NMR(CDCl ₃) ^b
17	H	O(CH ₂) ₂ CPh	Palely brown powder (70.5 %) 149.5-152 °C	(KBr) 2924, 1490, 1452, 1438, 1282, 1236, 1198, 1180, 1134, 1086, 1068, 930, 896, 832, 760,	1.38-2.03(6H,m), 2.66-2.93(2H,m), 3.25-3.55(2H,m), 4.29(4H,s), 6.62(1H,d,J=7Hz), 6.74-7.40(5H,m), 8.05(1H,d,J=7Hz)
18	H	[O] N	Colorless powder (62.0 %) 152-153 °C	(KBr) 2956, 2916, 2852, 1446, 1346, 1264, 1246, 1190, 1136, 1112, 1064, 1006, 988, 932, 890, 874, 856, 732,	1.50-2.49(6H,m), 2.70-3.23(6H,m), 3.23-3.65(2H,m), 3.72-4.00(4H,m), 6.67(1H,d,J=6Hz), 8.05(1H,d,J=6Hz)
19	H	SCH ₂ CH ₂ CH ₃	Colorless amorphous powder (79.6 %) —	(KBr) 3432, 3068, 2960, 2924, 2848, 2824, 1426, 1336, 1268, 1242, 1214, 1194, 1130, 1090, 1038, 1000, 880, 828, 742, 700, 634, 556,	1.06(3H,t,J=6Hz), 1.46-2.03(8H,m), 2.52-3.15(4H,m), 3.20-3.52(2H,m), 6.87(1H,d,J=6Hz), 8.02(1H,d,J=6Hz)
20	3-CH ₃	4-OCH ₂ CF ₂ CF ₂ H	Palely brown oily substance (100 %) —	(neat) 2932, 1455, 1419, 1296, 1272, 1248, 1224, 1197, 1170, 1110, 1068, 1050, 1032, 753,	1.50-2.01(6H,m), 2.19(2H,s), 2.69-2.95(2H,m), 3.20-3.50(2H,m), 4.11(2H,t,J=1Hz), 5.46, 6.05, 6.63(1H,tx3,J=4Hz), 7.98(1H,s)
21	H	OEt	Palely brown powder (74.3 %) 148-149.5 °C	(KBr) 3320, 2924, 1448, 1290, 1236, 1190, 1138, 1116, 1066, 1038, 894,	1.30-1.96(6H,m), 1.43(3H,t,J=7.5Hz), 2.69-2.96(2H,m), 3.26-3.53(2H,m), 4.02(2H,q,J=7.5Hz), 6.53(1H,d,J=9Hz), 8.04(1H,d,J=9Hz)
22	H	O-n-BU	Palely brown amorphous powder (54.8%) —	(KBr) 3384, 2952, 2852, 1450, 1406, 1290, 1240, 1198, 1188,	0.96(3H,t,J=7.5Hz), 1.16-2.35(10H,m), 2.73-3.05(2H,m), 3.18-3.56(2H,m), 3.94(2H,t,J=7.5Hz), 6.53(1H,d,J=9Hz), 8.03(1H,d,J=9Hz)

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Table 3 (3)

Reference Example No.	R	R ¹	Melting point (yield)	IR, μcm^{-1}	NMR (CDCl_3) δ
23	H		Palely brown oily substance (72.5 %) —	(neat) 3032, 2924, 1604, 1506, 1442, 1270, 1246, 1198, 1166,	1.33-2.20(6H, m), 2.32(3H, s), 2.73-3.06(2H, m), 3.28-3.56(2H, m), 6.43(1H, d, J=9Hz), 6.81(2H, d, J=10.5Hz), 7.15(2H, d, J=10.5Hz), 7.96(1H, d, J=9Hz)
24	H		Palely brown amorphous powder (92.6 %) —	(KBr) 3068, 2976, 2924, 1612, 1450, 1412, 1342, 1292, 1138, 1062, 1028,	0.19-0.81(4H, m), 1.03-1.36(1H, m), 1.40-2.06(6H, m), 2.71-3.03(2H, m), 3.24-3.58(2H, m), 3.80(2H, d, J=7.5Hz), 6.57(1H, d, J=9Hz), 8.04(1H, d, J=9Hz)
25	H		Palely brown oily substance (75.3 %) —	(neat) 3376, 2976, 2928, 2856, 1614, 1446, 1292, 1238, 1186, 1136, 1082, 1066,	1.35-2.23(10H, m), 2.54-2.96(2H, m), 3.23-3.57(2H, m), 3.65-4.06(4H, m), 4.06-4.43(1H, m), 6.58(1H, d, J=9Hz), 8.04(1H, d, J=9Hz)
26	β-CH ₃	H	Colorless powder (88.7%) —	(KBr) 3400, 2911, 2842, 1448, 1340, 1289, 1203, 1141, 1043,	1.50-1.97(6H, m), 2.20(3H, s), 2.62-2.87(2H, d, J=11Hz), 3.21-3.48(2H, d, J=11Hz), 6.80(1H, s), 7.97(1H, s)
27	β-CH ₃	OCH ₃	Palely brown powder (100 %) 108-109 °C	(KBr) 2932, 2818, 1479, 1460, 1404, 1344, 1296, 1250, 1198, 1006,	1.42-2.06(6H, m), 2.16(3H, s), 2.65-2.95(2H, m), 3.20-3.46(2H, m), 3.68(3H, s), 7.95(1H, s)
28	β-CH ₃	SCH ₂ CH ₂ CH ₃	Colorless amorphous powder (96.8%) —	(KBr) 2962, 2920, 2848, 1464, 1446, 1290, 1230, 1140, 651,	0.86-1.12(3H, t, J=7Hz), 1.30-2.02(8H, m), 1.40(3H, s), 1.48-1.73(2H, t, J=7Hz), 3.15-3.47(4H, m), 8.00(1H, s)

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Reference example 29

9-Acetoxy-2,3-cycloheptenopyridine

- 5 20 ml of acetic anhydride is added 4.9 g (30 mmol) of 2,3-cycloheptenopyridine-N-oxide, and the mixture is refluxed at 90 °C for 15 hours. After cooling, excessive acetic anhydride is distilled away under reduced pressure, and the resulting residue is extracted with ethyl acetate. The ethyl acetate layer is washed successively with a saturated aqueous sodium hydrogen carbonate solution and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The
 10 resulting residue is purified by silica gel column chromatography (ethyl acetate-n-hexane 1:3) to obtain 5.2 g (84.5 %) of 9-acetoxy-2,3-cycloheptenopyridine as a yellowish oily substance.

IR_vmax(neat): 3050, 2932, 2856, 1736, 1454, 1438, 1368, 1234, 1040 cm⁻¹.

NMR(CDCl₃)δ: 1.50-2.30(6H,m), 2.16(3H,m), 2.63-3.13(2H,m), 5.80-6.05 (1H,m), 6.90-7.47(2H,m), 8.31 (1H,d,J = 5Hz).

- 15 The compounds of the following Reference examples 30 to 32 are obtained in the same manner as above.

Reference example 30

20 9-Acetoxy-4-methoxy-2,3-cycloheptenopyridine

Yellowish oily substance

Yield: 76.5%

IR_vmax(neat): 2932, 2856, 1736, 1580, 1476, 1372, 1288, 1236, 1046, 966 818, 754 cm⁻¹.

25 NMR(CDCl₃)δ: 1.07-2.40(6H,m), 2.18(3H,m), 2.42-3.38(2H,m), 3.83(3H,s), 5.92(1H,bs), 6.67- (1H,d,J = 6Hz), 8.24(1H,d,J = 6Hz).

Reference example 31

30 9-Acetoxy-4-chloro-2,3-cycloheptenopyridine

Colorless oily substance

Yield: 53.2 %

IR_vmax(neat): 3045, 2936, 1742, 1558, 1452, 1370, 1234, 1054, 1026, 813 cm⁻¹.

35 NMR(CDCl₃)δ: 1.20-2.35(6H,m), 2.23(3H,s), 2.58-3.63(2H,m), 5.88-6.14 (1H,m), 7.26(1H,d,J = 5Hz), 8.24 (1H,d,J = 5Hz).

Reference example 32

40 9-Acetoxy-4-nitro-2,3-cycloheptenopyridine

Yellowish oily substance

Yield: 7.06 %

IR_vmax(neat): 3080, 2936, 2864, 1738, 1536, 1370, 1232, 1056, 842 cm⁻¹.

45 NMR(CDCl₃)δ: 1.38-2.26(6H,m), 2.18(3H,s), 2.40-3.32(2H,m), 5.84-6.13 (1H,m), 7.30(1H,d,J = 5Hz), 8.48- (1H,d,J = 5Hz).

Reference example 33

50 4-Ethoxy-9-hydroxy-3-methyl-2,3-cycloheptenopyridine

7.6 ml of Acetic anhydride is added to 1.12 g (5.00 mmol) of 4-ethoxy-3-methyl-2,3-cycloheptenopyridine-N-oxide, and the mixture is stirred at 90 °C for 1 hour and 40 minutes. After cooling, the reaction mixture is poured into ice water and neutralized with a 20 % aqueous sodium hydroxide solution, and the mixture is extracted with chloroform. The chloroform layer is washed successively with water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is dissolved in 24 ml of methanol, 14 ml of a 10 % aqueous sodium hydroxide solution is added under ice cooling, and the mixture is stirred at room temperature for 1

hour and 46 minutes. The reaction mixture is poured into ice water and extracted with methylene chloride. The methylene chloride layer is washed successively with water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is purified by silica gel column chromatography (chloroform-methanol 40:1) to obtain 1.02 g (91.9 %) of 4-ethoxy-9-hydroxy-3-methyl-2,3-cycloheptenopyridine as palely brown oily sustance.

5 IR_vmax(neat): 3364, 2974, 2926, 2854, 1590, 1569, 1443, 1425, 1395, 1290, 1263, 1230, 1209, 1098, 1047 918, 753 cm⁻¹.

10 NMR(CDCl₃)δ: 1.00-2.53(7H,m), 1.43(3H,t,J = 7Hz), 2.21(3H,s), 3.10-3.46 (1H,m), 3.84(2H,q,J = 7Hz), 4.67 (1H,d,J = 10Hz), 5.88(1H,bs), 8.10(1H,s).

10 Reference example 34

9-Hydroxy-4-methoxy-2,3-cycloheptenopyridine

15 910 mg (3.87 mmol) of 9-acetoxy-4-methoxy-2,3-cycloheptenopyridine is dissolved in methanol, a 10 % aqueous sodium hydroxide solution is added, and after stirring at room temperature for 1 hour, the mixture is refluxed at 80 °C for 10 minutes. After cooling, the methanol is distilled away under reduced pressure, and the resulting residue is extracted with methylene chloride. The methylene chloride layer is washed with saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under 20 reduced pressure. The resulting solid residue is recrystallized from ether-n-hexane to obtain 550 mg (73.5 %) of 9-hydroxy-4-methoxy-2,3-cycloheptenopyridine as yellowish prismatic crystals having a melting point of 119 to 120 °C.

IR_vmax(neat): 3312, 2984, 2982, 2852, 1590, 1478, 1450, 1398, 1284, 1260, 1050, 866, 824, 526 cm⁻¹.

NMR(CDCl₃)δ: 0.80-2.34(7H,m), 3.22-3.56 (1H,m), 3.84(3H,s), 4.72(1H,d,J = 11Hz), 6.69(1H,d,J = 6Hz),

25 8.23 (1H,d,J = 6Hz).

The compounds of the following Reference examples 35 and 36 are obtained in the same manner as above.

30 Reference example 35

9-Hydroxy-2,3-cycloheptenopyridine

Faintly yellow oily substance

Yield: 64.9 %

35 IR_vmax(neat): 3372, 2928, 2852, 1584, 1454, 1440, 1406, 1062, 796, 772 cm⁻¹.

NMR(CDCl₃)δ: 0.85-3.02(7H,m), 4.48-4.95 (1H,m), 5.88(1H,bs), 6.93-7.57 (2H,m), 8.32(1H,d,J = 5Hz).

Reference example 36

40 4-Chloro-9-hydroxy-2,3-cycloheptenopyridine

Colorless crystalline powder

Yield: 97.6 %

IR_vmax(KBr): 3400, 2924, 2852, 1564, 1454, 1422, 1380, 1064, 840, 778 cm⁻¹.

45 NMR(CDCl₃)δ: 0.80-2.70(7H,m), 3.47(1H,dd,J = 11Hz,J = 6Hz), 4.80(1H,d,J = 11Hz), 5.75(1H,bs), 7.18- (1H,d,J = 5Hz), 8.17(1H,d,J = 5Hz).

Reference example 37

50 9-Chloro-4-ethoxy-3-methyl-2,3-cycloheptenopyridine

In a stream of argon, 1.02 g (4.59 mmol) of 4-ethoxy-3-methyl-9-hydroxy-2,3-cycloheptenopyridine is dissolved in 6.5 ml of chloroform, 1.66 ml (23.0 mmol) of thionyl chloride is added dropwise with stirring at -12 °C, and after stirring at the same temperature for 30 minutes, the mixture is stirred at room temperature 55 for 16 hours. The reacion mixture is poured in ice water, neutralized with a saturated aqueous sodium hydrogen carbonate and extracted with chloroform. The chloroform layer is washed successively with water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure to obtain crude 9-chloro-4-ethoxy-3-methyl-2,3-cycloheptenopyridine as a palely brown

oily substance.

$\text{IR}_{\text{max}}(\text{neat})$: 2976, 2928, 2860, 1564, 1460, 1384, 1336, 1286, 1266, 1228, 1210, 1110, 1082, 1054, 1044, 1026, 958, 752, 736 cm^{-1} .

$\text{NMR}(\text{CDCl}_3)\delta$: 1.20-2.56(6H,m), 1.41(3H,t,J = 7Hz), 2.21(3H,s), 2.60-3.36 (2H,m), 3.81(2H,q,J = 7Hz), 5.41 (1H,d,J = 5Hz), 8.06(1H,s).

Reference 38

9-Bromo-2,3-cycloheptenopyridine

10 1.13 g (8.16 mmol) of 9-hydroxy-2,3-cycloheptenopyridine is dissolved in 10 ml of dry benzene, 0.28 ml of phosphorus tribromide is added dropwise under ice cooling and stirring, and the mixture is stirred overnight at room temperature. After the reaction, ice water is added for cooling, and the mixture is neutralized with 1N sodium hydroxide and extracted with methylene chloride. The methylene chloride layer is washed with saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is purified by silica gel column chromatography (chloroform-methanol 200:1) to obtain 391 mg (21.3 %) of 9-bromo-2,3-cycloheptenopyridine as yellowish oily substance.

$\text{IR}_{\text{max}}(\text{neat})$: 3045, 2928, 2856, 1754, 1452, 1440, 1186, 964, 792, 776 698, 682 cm^{-1} .

20 $\text{NMR}(\text{CDCl}_3)\delta$: 1.02-3.50(8H,m), 5.58(1H,d,J = 5Hz), 6.94-7.67(2H,m), 8.28 (1H,d,J = 5Hz).
The compounds of Table-3 can be halogenated in the same manner as in the above Reference examples 33 to 37.

Example 1

25 9-(5-Methoxybenzimidazole-1-yl)thio-2,3-cycloheptenopyridine

30 303 mg (1.68 mmol) of 2-mercapto-5-methoxybenzimidazole is dissolved in an aqueous sodium hydroxide solution (wherein 80 mg of sodium hydroxide is dissolved in 1.4 ml of water) and 10 ml of methanol, 379 mg (1.68 mmol) of 9-bromo-2,3-cycloheptenopyridine is added thereto with stirring at room temperature, and the mixture is refluxed for 1.5 hours. After cooling, the methanol is distilled away under reduced pressure, and the residue is extracted with methylene chloride. The methylene chloride layer is washed with saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting oily residue is purified by silica gel column chromatography (chloroform) and recrystallized from chloroform-n-hexane to obtain 355 mg (64.9 %) of 9-(5-methoxybenzimidazole-2-yl)thio-2,3-cycloheptenopyridine as colorless granular crystals having a melting point of 157 to 158 °C.

$\text{IR}_{\text{max}}(\text{KBr})$: 2924, 1625, 1452, 1434, 1396, 1158 cm^{-1} .

35 $\text{NMR}(\text{CDCl}_3)\delta$: 1.34-2.45(6H,m), 2.60-3.34 (2H,m), 5.08(1H,d,J = 6Hz), 6.63-7.56(5H,m), 8.35-40 (1H,d,J = 5Hz).

The compound of the following Example 2 is obtained in the same manner as above.

Example 2

45 9-(Benzimidazole-2-yl)thio-2,3-cycloheptenopyridine

Colorless minute needle crystals

Melting point: 281 to 282 °C

Yield: 63.4 %

50 $\text{IR}_{\text{max}}(\text{KBr})$: 2924, 2852, 2788, 2696, 2632, 1454, 1438, 1398, 1348, 1270, 746 cm^{-1} .

$\text{NMR}(\text{CDCl}_3-\text{DMSO-D}_6)\delta$: 1.53-2.46(6H,m), 3.35 -3.67(2H,m), 5.29-5.65(1H,br), 6.98-7.77(6H,m), 8.30- (1H,d,J = 5Hz).

Example 3

9-(5-nitrobenzimidazole-2-yl)thio-2,3-cycloheptenopyridine

5 327 mg (2 mmol) of 9-hydroxy-2,3-cycloheptenopyridine is dissolved in 3 ml of chloroform from which ethanol is removed, 0.73 ml (10 mmol) of thionyl chloride is added dropwise with cooling at -15 °C, and the mixture is stirred overnight at room temperature. After the reaction, the solvent is distilled away under reduced pressure, the residue is dissolved in methylene chloride, the solution is washed with saturated sodium hydrogen carbonate, and the solvent is distilled away to obtain crude 9-chloro-2,3-cycloheptenopyridine.

10 The crude 9-chloro-2,3-cycloheptenopyridine is dissolved in 5 ml of ethanol, the solution is added to ethanol (10 ml) - an aqueous sodium hydroxide solution (wherein 120 mg of sodium hydroxide is dissolved in 2 ml of water), containing 303 mg (1.68 mmol) of 2-mercapto-5-nitrobenzimidazole, and the resulting mixture is refluxed for 21 hours. After the reaction, the ethanol is distilled away under reduced pressure, and the resulting residue is extracted with chloroform. The chloroform layer is washed with saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting oily residue is purified by silica gel column chromatography (chloroform) and recrystallized from ethyl acetate-n-hexane to obtain 359 mg (52.7 %) of 9-(5-nitrobenzimidazole-2-yl)thio-2,3-cycloheptenopyridine as colorless granular crystals having a melting point of 222 to 223 °C.

20 IR_vmax(KBr): 3072, 2928, 2852, 1514, 1452, 1432, 1332, 1276, 1066, 736 cm⁻¹.

NMR(CDCl₃)δ: 1.54-3.34(8H,m), 5.17(1H,bs), 7.02-7.68(3H,m), 7.92-8.48 (3H,m).

The compounds of the following Examples 4 to 7 are obtained in the same manner as above.

Example 4

9-(5-Chlorobenzimidazole-2-yl)thio-2,3-cycloheptenopyridine

Yellowish candy-like substance

Yield: 78.8 %

30 IR_vmax(neat): 3056, 2932, 2856, 1452, 1432, 1406, 1332, 1266, 1060, 992 754 cm⁻¹.

NMR(CDCl₃)δ: 1.42-3.43(8H,m), 5.12(1H,bs), 6.94-8.85(5H,m), 8.35(1H,d,J = 5Hz).

Example 5

9-(5-Fluorobenzimidazole-2-yl)thio-2,3-cycloheptenopyridine

Colorless powder

Melting point: 202 to 203 °C

Yield: 53.6 %

40 IR_vmax(KBr): 3036, 2924, 2848, 1482, 1436, 1396, 1345, 1262, 1216, 1142 988, 960, 836, 802 cm⁻¹.

NMR(CDCl₃)δ: 1.30-2.53(6H,m), 2.55-3.43 (2H,m), 4.95-5.33(1H,m), 6.66-7.68(5H,m), 8.32(1H,d,J = 3Hz).

Example 6

9-(5-Methylbenzimidazole-2-yl)thio-2,3-cycloheptenopyridine

Palely yellow powder

Melting point: 207 to 208.5 °C

Yield: 44.9 %

50 IR_vmax(KBr) : 2924, 2848, 2784, 2616, 1434, 1390, 1276, 800 cm⁻¹.

NMR(CDCl₃)δ: 1.40-2.43(6H,m), 2.41(3H,s), 2.60-3.40(2H,m), 4.97-5.23 (1H,m), 6.76-7.62(5H,m), 8.35 (1H,d,J = 4Hz).

Example 7

9-(5-Trifluoromethylbenzimidazole-2-yl)thio-2,3-cycloheptenopyridine

5 Pale yellow amorphous powder

Yield: 53.1 %

IR_vmax(KBr): 2932, 1452, 1432, 1328, 1280, 1246, 1160, 1116, 1050, 756 cm⁻¹.NMR(CDCl₃)δ: 1.43-2.50(6H,m), 2.56-3.23 (2H,m), 5.23(1H,bs), 6.96-7.93 (5H,m), 8.17-8.53(1H,m).10 Example 8

9-(5-Methoxybenzimidazole-2-yl)thio-4-methoxy-2,3-cycloheptenopyridine

700 mg (3.62 mmol) of 9-hydroxy-4-methoxy-2,3-cycloheptenopyridine is dissolved in 6 ml of chloroform from which ethanol is removed, 1.3 ml (17.9 mmol) of thionyl chloride is added dropwise under cooling at -15 °C, and the mixture is stirred overnight at room temperature. After the reaction, the solvent is distilled away under reduced pressure, the residue is dissolved in methylene chloride, the resulting solution is washed with saturated sodium hydrogen carbonate, and the solvent is distilled away to obtain crude 9-chloro-4-methoxy-2,3-cycloheptenopyridine.

20 The crude 9-chloro-4-methoxy-2,3-cycloheptenopyridine is dissolved in 5 ml of ethanol, the solution is added to previously prepared ethanol (2 ml) - an aqueous sodium hydroxide solution (wherein 290 mg of sodium hydroxide is dissolved in 4.5 ml of water), containing 783mg (4.34 mmol) of 2-mercapto-5-methoxybenzimidazole, and the resulting mixture is refluxed for 4.5 hours. After the reaction, the ethanol is distilled away under reduced pressure, and the resulting residue is extracted with methylene chloride. The 25 methylene chloride layer is washed with saturated saline and dried over magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting solid residue is purified by alumina column chromatography (ethyl acetate-n-hexane 1:3) to obtain 940 mg (73.0 %) of 9-(5-methoxybenzimidazole-2-yl)-thio-4-methoxy-2,3-cycloheptenopyridine as colorless amorphous powder.

IR_vmax(KBr): 2924, 2840, 1578, 1432, 1288, 1152, 814 cm⁻¹.30 NMR(CDCl₃)δ: 1.22-2.39(6H,m), 2.74-3.36 (2H,m), 3.79, 3.82(each 3H,s), 5.06(1H,t,J = 4Hz), 6.62-7.60 (3H,m), 6.70(1H,d,J = 6Hz), 8.25 (1H,d,J = 6Hz).

The compounds of the following Examples 9 to 11 are obtained in the same manner as above.

Example 9

9-(Benzimidazole-2-yl)thio-4-methoxy-2,3-cycloheptenopyridine

Colorless powder

Melting point: 176 to 179 °C

40 Yield: 69.8 %

IR_vmax(KBr): 3044, 2920, 1578, 1436, 1406, 1156, 810, 752 cm⁻¹.NMR(CDCl₃)δ: 1.14(6H,m), 2.45-3.47(2H,m), 3.82(3H,s), 5.10(1H,t,J = 4Hz), 6.68(1H,d,J = 6Hz), 6.97-7.30 (2H,m), 7.30-7.63(2H,m), 8.24 (1H,d,J = 6Hz).45 Example 10

9-(5-Fluorobenzimidazole-2-yl)thio-4-methoxy-2,3-cycloheptenopyridine

Yellowish powder

50 Melting point: 93 to 95 °C

Yield: 74.8 %

IR_vmax(KBr): 3045, 2976, 2928, 1628, 1580, 1438, 1290, 1134, 1052, 838 cm⁻¹.NMR(CDCl₃)δ: 1.15-2.43(6H,m), 2.53-3.50 (2H,m), 3.83(3H,s), 5.08(1H,bs), 6.54-7.52(3H,m), 6.72- (1H,d,J = 6Hz), 8.25(1H,d,J = 6Hz).

Example 11

9-(5-Methoxybenzimidazole-2-yl)thio-4-chloro-2,3-cycloheptenopyridine

5 Colorless powder
 Melting point: 113 to 116 °C
 Yield: 63.4 %
 IR_vmax(KBr): 2928, 1625, 1560, 1490, 1456, 1432, 1404, 1346, 1200, 1154, 834 cm⁻¹.
 NMR(CDCl₃)δ: 1.40-2.52(6H,m), 3.07-3.38 (2H,m), 3.80(3H,s), 5.06-5.33 (1H,m), 6.63-7.60(4H,m), 8.20
 10 (1H,d,J=5Hz).

Example 12

9-(Benzimidazole-2-yl)thio-4-(2-hydroxyethoxy)-2,3-cycloheptenopyridine

15 In a stream of argon, 1.48 g (3.32 mmol) of 9-(benzimidazole-2-yl)thio-4-(2-benzyloxyethoxy)-2,3-cycloheptenopyridine is suspended in 7.5 ml of methylene chloride, 7.5 ml of dimethyl sulfide is added and dissolved under ice cooling and stirring, 3.75 ml (30.5 mmol) of a trifluoroborane-ether complex is added dropwise, and the resulting mixture is stirred for 30 minutes under ice cooling and further for 12 hours at room temperature. After completion of the reaction, the reaction mixture is poured into ice water, and the resulting mixture is made weakly alkaline with potassium carbonate and extracted with chloroform. The chloroform layer is washed successively with water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is separated and purified by silica gel column chromatography (chloroform-methanol 30:1) to obtain 1.18 g (99.8 %) of 9-(benzimidazole-2-yl)thio-4-(2-hydroxyethoxy)-2,3-cycloheptenopyridine as colorless amorphous powder.
 IR_vmax(KBr): 3154, 3064, 2926, 2854, 1581, 1470, 1437, 1407, 1350, 1290, 1269, 1230, 1092, 1053, 903, 813, 741 cm⁻¹.
 NMR(CDCl₃)δ: 1.20-3.40(8H,m), 3.95-4.35 (4H,m), 4.96-5.20(1H,m), 6.70 (1H,d,J=6Hz), 6.99-7.55-
 30 (4H,m), 8.22(1H,d,J=6Hz).

Example 13

4-(2-Acetoxyethoxy)-9-(benzimidazole-2-yl)thio-2,3-cycloheptenopyridine

35 In a stream of argon, 573 mg (1.44 mmol) of 9-(benzimidazole-2-yl)thio-4-(2-hydroxyethoxy)-2,3-cycloheptenopyridine is dissolved in 6 ml of methylene chloride, 0.46 ml (5.76 mmol) of pyridine is added dropwise with stirring at room temperature and successively 0.27 ml (2.88 mmol) of acetic anhydride is added dropwise, and the resulting mixture is stirred at room temperature for 14 hours and 30 minutes. After cooling, the reaction mixture is poured into ice water, followed by extraction with chloroform. The chloroform layer is washed successively with water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is purified by silica gel column chromatography (chloroform-methanol 30:1). The resulting oily substance is dissolved in methylene chloride, 7.28 g of silica gel is added, the mixture is stirred at room temperature for 1 hour, the silica gel is filtered off, and then the methylene chloride is distilled away under reduced pressure to obtain 520 mg (90.9 %) of 9-(benzimidazole-2-yl)thio-4-(2-acetoxyethoxy)-2,3-cycloheptenopyridine as a colorless oily substance.
 IR_vmax(Neat): 2928, 1740, 1580, 1470, 1452, 1438, 1406, 1290, 1268, 1228, 1094, 1058, 908, 736, 648, 604 cm⁻¹.
 50 NMR(CDCl₃)δ: 1.18-2.42(6H,m), 2.70(3H,s), 2.56-3.41(2H,m), 4.06-4.30 (2H,m), 4.30-4.54(2H,m), 4.99-
 5.22(1H,m), 6.69(1H,d,J=6Hz), 6.96-7.26(2H,m), 7.30-7.62 (2H,m), 8.24(1H,d,J=6Hz).

Example 14

55 4-Ethoxy-9-(5-methoxybenzimidazole-2-yl)thio-3-methyl-2,3-cycloheptenopyridine

Crude 9-chloro-4-ethoxy-3-methyl-2,3-cycloheptenopyridine (4.95 mmol) is dissolved in 16 ml of ethanol, 892 mg (4.95 mmol) of 5-methoxy-2-mercaptopbenzimidazole and 16 ml of a 20 % aqueous sodium

hydroxide solution are added, and the mixture is refluxed with heating for 20 hours. After cooling, the solvent is distilled away under reduced pressure and the residue is extracted with chloroform. The chloroform layer is washed successively with a saturated aqueous sodium hydrogen carbonate solution, water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is subjected to active alumina column chromatography (ethyl acetate : hexane 2:3 → ethyl acetate → ethyl acetate : methanol 100:1) to obtain 799 mg (42.1 %) of 4-ethoxy-9-(5-methoxybenzimidazole-2-yl)thio-3-methyl-2,3-cycloheptenopyridine as colorless amorphous powder.

5 IR_vmax(KBr): 2976, 2924, 2852, 1626, 1450, 1398, 1344, 1288, 1268, 1228, 1200, 1154, 1052, 1026, 960, 838, 802 cm⁻¹.

10 NMR(CDCl₃)δ: 1.10-2.40(6H,m), 1.43(3H,t,J = 7Hz), 2.23(3H,s), 2.65-3.33 (2H,m), 3.65-4.03(2H,m), 3.81 (3H,s), 4.93-5.16(1H,m), 6.65-7.65(3H,m), 8.14(1H,s).

Example 15

15 9-[1-Benzoyloxycarbonyl]benzimidazole-2-yl]thio-4-methoxy-2,3-cycloheptenopyridine

In a stream of argon, 520 mg (1.60 mmol) of 9-(benzimidazole-2-yl)thio-4-methoxy-2,3-cycloheptenopyridine is dissolved in 10 ml of THF, 215 mg (1.90 mmol) of potassium t-butoxide (t-BuOK) dissolved in 20 8 ml of THF is added dropwise under ice cooling and stirring, and the mixture is stirred at room temperature for 20 minutes. Then, 607 mg (3.20 mmol) of carbobenzoxy chloride dissolved in 2 ml of THF is added dropwise, and the mixture is stirred at room temperature for 30 minutes. After completion of the reaction, a saturated aqueous ammonium chloride solution is added to the reaction mixture, followed by extraction with methylene chloride. The methylene chloride layer is washed successively with water and 25 saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is crystallized from chloroform-hexane to obtain 657 mg (89.5 %) of 9-[1-(benzoyloxycarbonyl)benzimidazole-2-yl]thio-4-methoxy-2,3-cycloheptenopyridine as colorless powder having a melting point of 181 to 184 °C.

IR_vmax(KBr): 3430, 2910, 1736, 1576, 1466, 1450, 1392, 1332, 1294, 1280, 1254, 1194, 1078 cm⁻¹.
30 NMR(CDCl₃)δ: 1.36-2.94(7H,m), 3.06-3.33 (1H,m), 3.82(3H,s), 5.50(2H,s), 5.66(1H,d,J = 9.0Hz), 6.65- (1H,d,J = 7.5Hz), 6.97-7.86(9H,m), 8.23 (1H,d,J = 7.5Hz).

Example 16

35 9-[1-(hydroxymethyl)benzimidazole-2-yl]thio-4-methoxy-2,3-cycloheptenopyridine

958 mg (2.95 mmol) of 9-(benzimidazole-2-yl)thio-4-methoxy-2,3-cycloheptenopyridine is dissolved in 16 ml of acetonitrile and 16 ml of methylene chloride, and under stirring 0.36 ml (4.42 mmol) of 37 % formaldehyde dissolved in 1 ml of acetonitrile is added dropwise. The mixture is then stirred for 30 minutes 40 and further at 70 °C for 45 minutes. The reaction mixture is poured into ice water, followed by extraction with methylene chloride. The methylene chloride layer is washed successively with water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is crystallized from methylene chloride-hexane to obtain 676 mg (64.6 %) of 9-[1-(hydroxymethyl)benzimidazole-2-yl]thio-4-methoxy-2,3-cycloheptenopyridine as colorless powder having a melting point of 136 to 138 °C. The mother liquor is evaporated under reduced pressure, and the resulting residue is crystallized from methylene chloride-ether-hexane to obtain 246 mg (23.5 %) of the above compound (total yield 88.1 %).

IR_vmax(KBr): 3132, 2968, 2936, 1578, 1474, 1466, 1428, 1366, 1330, 1304, 1288, 1250, 1136, 1102, 1082 cm⁻¹.
50 NMR(CDCl₃)δ: 1.33-3.20(8H,m), 3.80(3H,s), 4.81-5.16(1H,m), 5.73(2H,q,J = 9Hz), 6.60(1H,d,J = 7.5Hz), 7.03-7.86(4H,m), 8.00(1H,d,J = 7.5Hz).

Example 17

55 9-[1-(t-Butoxycarbonylmethoxymethyl)benzimidazole-2-yl]thio-4-methoxy-2,3-cycloheptenopyridine

In a stream of argon, 48 mg (1.20 mmol) of 60 % sodium hydride is suspended in 5 ml of THF, and under ice cooling and stirring, 355 mg (1.00 mmol) of 9-[1-(hydroxymethyl)benzimidazole-2-yl]thio-4-

methoxy-2,3-cycloheptenopyridine dissolved in 5 ml of THF is dropwise added by portions. The resulting mixture is stirred at room temperature for 45 minutes. Then, under ice cooling and stirring, t-butoxycarbonyl bromide dissolved in 2 ml of THF is added dropwise, and the mixture is stirred at room temperature for 16 hours. After the reaction, the reaction mixture is poured into a saturated aqueous ammonium chloride solution, followed by extraction with methylene chloride. The methylene chloride layer is washed successively with water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure to obtain 427 mg (91.2 %) 9-[1-(t-butoxycarbonylmethoxymethyl)-benzimidazole-2-yl]thio-4-methoxy-2,3-cycloheptenopyridine

5
10 IR_vmax(KBr): 2976, 2928, 1744, 1626, 1578, 1474, 1444, 1368, 1334, 1314, 1282, 1232, 1156, 1114, 1092 cm⁻¹.

10 NMR(CDCl₃) δ : 1.40(9H,s), 1.60-2.80(7H,m), 3.16-3.46(1H,m), 3.83(3H,s) 4.83(2H,s), 5.50-5.75(1H,m), 5.70(2H,s), 6.67(1H,d,J = 7.5Hz), 7.04-7.80(4H,m), 8.10-8.28 (1H,d,J = 7.5Hz).

Example 18

15 9-[pyrido[2,3-d]imidazole-2-yl]thio-2,3-cycloheptenopyridine

Crude 9-chloro-2,3-cycloheptenopyridine (9.15 mmol) is dissolved in 29 ml of ethanol, 1.38 g (9.15 mmol) of 2-mercaptopyrido [2,3-d] imidazole and 29 ml of a 20 % aqueous sodium hydroxide solution are 20 added thereto, and the mixture is refluxed with heating for 20 hours. After cooling, the solvent is distilled away under reduced pressure, and the residue is extracted with chloroform. The chloroform layer is washed successively with a saturated aqueous sodium hydrogen carbonate solution, water and saturated saline, and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is subjected to activated alumina column chromatography (ethyl acetate : hexane 2:3 → 25 ethyl acetate → ethyl acetate : methanol 100:1) to obtain 700 mg (25.8 %) of 9-[pyrido[2,3-d]imidazole-2-yl]thio-2,3-cycloheptenopyridine as colorless amorphous powder.

IR_vmax(KBr): 2921, 1452, 1439, 1393, 1268, 768, 753 cm⁻¹.

NMR(CDCl₃) δ : 1.39-2.60(6H,m), 2.60-3.30 (2H,m), 5.13-5.33(1H,m), 6.97-7.30(2H,m), 7.31-7.60(1H,m), 7.56-7.92(1H,m), 8.15-8.50 (2H,m).

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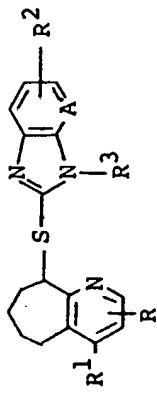
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The compounds in Table-4 are obtained in the same manner as in Examples 1 to 18.

Table-4 (1) a



Example No.	R	R ¹	R ²	R ³	A	Melting point (yield)
19	H	OEt	H	H	CH	Colorless amorphous powder (74.2 %) ---
20	H	O-n-Bu	H	H	CH	Colorless powder (55.8 %) 65-70 °C
21	H	O-C ₆ H ₄ -CH ₃	H	H	CH	Pale yellow needle crystal (55.4 %) 222-223 °C
22	H	O-C ₃ H ₅	H	H	CH	Colorless powder (46.4 %) 159-160 °C
23	H	O-C ₃ H ₅ O	H	H	CH	Colorless amorphous powder (82.9 %) ---
24	H	OCH ₃	H	CH ₂ OOCCH ₃	CH	Colorless powder (61.1 %) 160-162 °C

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Table-4 (1)b

Example No.	IR\cm ⁻¹	NMR (CDCl ₃) ^δ
19	(KBr) 3432, 2976, 2924, 1464, 1438, 1290, 1268, 1232, 1088, 8.22(1H,d,J=9Hz)	1.43(3H,t,J=7.5Hz), 1.66-3.32(8H,m), 4.03(2H,q,J=7.5Hz), 5.19(1H,t,J=6Hz), 6.65(1H,d,J=9Hz), 6.96-7.66(4H,m), 8.22(1H,d,J=9Hz)
20	(KBr) 3429, 3064, 2928, 1580, 1460, 1438, 1288, 1268, 1088, 8.22(1H,d,J=9Hz)	0.96(3H,t,J=7.5Hz), 1.12-2.43(10H,m), 2.60-3.31(2H,m), 3.96(2H,t,J=7.5Hz), 5.18(1H,t,J=6Hz), 6.66(1H,d,J=7.5Hz), 6.86-8.64(4H,m), 8.22(1H,d,J=7.5Hz)
21	(KBr) 3430, 2928, 1576, 1460, 1438, 1398, 1348, 1332, 1270, 1250, 1204, 1162, J=7.5Hz)	1.36-3.55(8H,m), 2.33(3H,s), 5.03-5.30 (1H,m), 6.50(1H,d,J=7.5Hz), 6.84(2H,d, J=7.5Hz), 6.96-7.66(6H,m), 8.13(1H,d, J=7.5Hz)
22	(KBr) 3460, 3080, 3032, 2960, 2924, 1582, 1462, 1450, 1430, 1404, 1350, 1272, 1042, 1008, 8.23(1H,d,J=7.5Hz)	0.13-0.76(4H,m), 1.10-1.64(1H,m), 1.66-3.46(8H,m), 3.83(1H,d,J=7.5Hz), 5.10(1H,t,J=6Hz), 6.65(1H,d,J=7.5Hz), 6.97-7.64(4H,m), 8.22(1H,d,J=7.5Hz)
23	(KBr) 2972, 2928, 2860, 1578, 1438, 1406, 1346, 1290, 1268, 1230, 1082, 1050, 8.23(1H,d,J=7.5Hz)	1.36-2.53(10H,m), 2.64-3.36(1H,m), 3.73-4.36(5H,m), 5.08(1H,t,J=6Hz), 6.70(1H,d,J=7.5Hz), 6.94-7.76(4H,m), 8.23(1H,d,J=7.5Hz)
24	(KBr) 2924, 1750, 1578, 1472, 1440, 1352, 1280, 1260, 1212, 1052, 1018, 8.23(1H,d,J=7.5Hz)	1.63-2.85(7H,m), 2.03(3H,s), 3.07-3.46 (1H,m), 3.83(3H,s), 5.64(1H,d,J=10.5 Hz), 6.15(2H,d,d,J=30Hz,J=30Hz), 6.67 (1H,d,J=7.5Hz), 7.06-7.76(4H,m), 8.23 (1H,d,J=7.5Hz)

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Table-4 (2)a

Example No.	R	R ¹	R ²	R ³	A	Melting Point (yield)
25	H	OCH ₃	H	CH ₂ OCH ₃	CH	Colorless amorphous powder (71.0 %) ---
26	H	OCH ₃	H	CH ₂ OEt	CH	Colorless candy-like substance (66.8 %) ---
27	H	OCH ₃	H	CH ₂ O(CH ₂) ₂ OCH ₃	CH	Colorless candy-like substance (91.7 %) ---
28	H	OCH ₃	H	COO(CH ₂) ₂ OCH ₃	CH	Palely yellow powder (90.6 %) 150-151 °C
29	H	OCH ₂ CF ₂ CF ₃	H	H	CH	Colorless amorphous powder (58.1 %) ---
30	H	OCH ₂ CF ₂ CF ₂ H	H	H	CH	Colorless amorphous powder (51.7 %) ---
31	H	OCH ₂ Ph	H	H	CH	Colorless amorphous powder (65.0 %) ---

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Table-4 (2) b

Example No.	IR/cm ⁻¹	NMR(CDCl ₃)δ
25	(KBr) 2928, 2852, 1578, 1432, 1334, 1283, 1268, 1112, 1092, 1056,	1.56-2.86(7H,m), 3.10-3.46(1H,m), 3.29 (3H,s), 3.83(3H,s), 5.52(2H,s), 5.68, (1H,d,J=9Hz), 6.66(1H,d,J=7.5Hz), 7.06-7.78(4H,m), 8.22(1H,d,J=7.5Hz)
26	(neat) 2976, 2928, 2856, 1578, 1474, 1434, 1394, 1264, 1092, 1056, 942,	1.43(3H,t,J=9Hz), 1.62-2.43(7H,m), 2.46-2.85(1H,m), 3.50(2H,q,J=9Hz), 3.80(3H,s), 5.55(2H,s), 5.67(1H,d,J= 10.5Hz), 6.65(1H,d,J=7.5Hz), 7.06-7.75 (4H,m), 8.22(1H,d,J=7.5Hz)
27	(KBr) 2924, 2852, 1578, 1472, 1332, 1282, 1264, 1134, 1090, 1056,	1.54-2.86(8H,m), 3.14-3.84(4H,m), 3.29 (3H,s), 3.81(3H,s), 3.50-3.81(1H,m), 3.51(2H,m), 6.64(1H,d,J=7.5Hz), 7.05- 7.73(4H,m), 8.11(1H,m)
28	(KBr) 2920, 2848, 1746, 1578, 1452, 1406, 1384, 1332, 1264, 1192, 1138, 1076,	1.62-2.94(8H,m), 3.43(3H,s), 3.76(2H, t,J=6Hz), 3.82(3H,s), 4.62(2H,t,J=6Hz), 5.53-5.83(1H,m), 6.65(1H,d,J=7.5Hz), 7.04-7.98(4H,m), 8.22(1H,d,J=7.5Hz)
29	(KBr) 2928, 1578, 1440, 1404, 1350, 1294, 1268, 1198, 1152, 1100, 740	1.13-2.40(6H,m), 2.70-3.38(2H,m), 4.46 (2H,t,J=12Hz), 5.20(1H,t,J=4Hz), 6.69 (1H,t,J=5Hz), 7.00-7.78(4H,m), 8.33 (1H,d,J=5Hz)
30	(KBr) 3064, 2929, 2856, 1578, 1470, 1454, 1438, 1404, 1348, 1312, 1290, 1268, 1228, 1200, 1106, 1062, 942, 836, 810, 742,	1.10-2.42(6H,m), 2.73-3.35(2H,m), 4.38 (2H,m), 5.18(1H,br), 5.38, 5.98, 6.57 (1H,tx3,J=3Hz), 6.70(1H,d,J=6Hz), 7.00-7.75(4H,m), 8.32(1H,d,J=6Hz)
31		1.15-2.45(6H,m), 2.63-3.40(2H,m), 5.05(2H,s), 5.20(1H,t,J=4Hz), 6.70 (1H,d,J=5Hz), 7.10-7.95(4H,m), 7.31 (5H,s), 8.21(1H,d,J=5Hz)

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Table-4 (3) a

Example No.	R	R ¹	R ²	R ³	A	Melting point (yield)
32	H	SCH ₂ CH ₂ CH ₃	H	H	CH	Colorless amorphous powder (42.0 %) ---
33	H		H	H	CH	Colorless powder (56.4 %) 215-217 °C
34	H	OCH ₂ CH ₂ OCH ₃	5-F	H	CH	Colorless powder (43.6 %) 141-142 °C
35	H	OCH ₃	5,6-OCH ₃	H	CH	Colorless powder (38.9 %) 112-114.5 °C
36	H	OCH ₂ CF ₃	H	H	CH	Palely Yellow amorphous powder (47.6 %) ---
37	H	OCH ₂ CH=CH ₂	H	H	CH	Colorless powder (51.6 %) 106-108 °C
38	H	OCH ₂ CH ₂ OCH ₃	H	H	CH	Colorless powder (56.3 %) 124-125 °C
39	H	O(CH ₂) ₃ OCH ₃	H	H	CH	Colorless amorphous powder (38.5 %) ---

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Table-4 (3)b

Example No.	IR\cm ⁻¹	NMR (CDCl ₃) ^a
32		1.08(3H, t, J=7Hz), 1.20-3.68(12H, m), 5.20(1H, br), 6.97(1H, d, J=5Hz), 7.00-7.95(4H, m), 8.21(1H, d, J=5Hz),
33	(KBr) 2960, 2924, 2852, 1580, 1446, 1420, 1394, 1342, 1270, 1252, 1116, 988, 904, 740,	1.08-2.47(6H, m), 2.73-3.35(6H, m), 4.05(4H, m), 5.04-5.25(1H, m), 6.80(1H, d, J =6Hz), 7.00-7.76(4H, m), 8.26(1H, d, J=6Hz)
34	(KBr) 2928, 2856, 1582, 1474, 1432, 1404, 1346, 1286, 1260, 1230, 1196, 1130, 1110, 1084, 1056, 1036, 966, 952, 800,	1.13-2.53(6H, m), 2.63-3.30(2H, m), 3.42(3H, s), 3.63-3.86(2H, m), 4.02-4.24(2H, m), 4.98-5.20(1H, m), 6.72(1H, d, J=7Hz), 6.76- 7.57(3H, m), 8.22(1H, d, J=7Hz)
35	(KBr) 2932, 1578, 1488, 1472, 1440, 1420, 1398, 1328, 1282, 1196, 1170, 1136,	1.03-2.35(6H, m), 2.63(2H, m), 3.84(3H, s), 3.88(6H, s), 4.86-5.10(1H, m), 6.70(1H, d, J =6Hz), 6.75-7.16(2H, m), 8.25(1H, d, J=6Hz)
36	(KBr) 3064, 2856, 1578, 1470, 1454, 1438, 1404, 1348, 1316, 1290, 1264, 1230, 1166, 1138, 1100, 1064, 974,	1.40-2.50(6H, m), 2.71-3.41(2H, m), 4.37(2H, q, J=9Hz), 5.03-5.26(1H, m), 6.67(1H, d, J=6Hz), 7.00-7.70(4H, m), 8.30(1H, d, J=6Hz)
37	(KBr) 2924, 2852, 1578, 1468, 1436, 1404, 1346, 1310, 1282, 1268, 1230, 1044, 1016, 930, 816, 740,	1.05-2.36(6H, m), 2.65-3.36(2H, m), 4.50(2H, d, J=4Hz), 4.96-5.36(2H, m), 5.37(1H, d, J=9Hz), 5.66-6.23(1H, m), 6.63(1H, d, J=5Hz), 6.93-7.30(2H, m), 7.30-7.60(2H, m), 8.18(1H, d, J=5Hz)
38	(KBr) 2976, 2924, 2852, 1578, 1470, 1438, 1402, 1288, 1266, 1234, 1196, 1128, 1088, 1056, 740,	1.33-2.35(6H, m), 2.65-3.23(2H, m), 3.39 (3H, s), 3.56-3.83(2H, m), 3.93-4.25(2H, m), 5.02-5.26(1H, m), 6.68(1H, d, J=6Hz), 6.93-7.28(2H, m), 7.28-7.62(2H, m), 8.21(1H, d, J=6Hz)
39	(KBr) 2924, 2856, 1578, 1460, 1438, 1400, 1286, 1266, 1228, 1116, 1088, 1050, 814, 738,	1.13-2.40(8H, m), 2.57-3.20(2H, m), 3.30 (3H, s), 3.51(2H, t, J=6Hz), 4.07(2H, t, J=6Hz), 6Hz), 4.99-5.17(1H, m), 6.69(1H, d, J=6Hz), 6.95-7.78(4H, m), 8.22(1H, d, J=6Hz)

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Table-4 (4)a

Example No.	R	R ¹	R ²	R ³	A	Melting point (yield)
40	H	O(CH ₂) ₂ OCH ₂ Ph	H	H	CH	Colorless powder (52.5 %) 168-169 C
41	H	O(CH ₂) ₂ OPh	H	H	CH	Colorless amorphous powder (50.9 %) ---
42	H	O(CH ₂) ₂ OCH ₂ PY	H	H	CH	Colorless amorphous powder (32.8 %) ---
43	H	O(CH ₂) ₂ N(=O)C(=O)O	H	H	CH	Colorless amorphous powder (36.5 %) ---
44	3-CH ₃	4-OCH ₂ CF ₂ CF ₂ H	5-F	H	CH	Palely yellow amorphous powder (55.8 %) ---
45	3-CH ₃	4-OCH ₃	5-OCH ₃	H	CH	Yellow amorphous powder (36.8 %) ---
46	H	OCH ₂ CH ₂ OCH ₃	5-CH ₃	H	CH	Palely yellow amorphous powder (37.6 %) ---

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Table-4 (4)b

Example No.	IR ν cm $^{-1}$	NMR(CDCl $_3$) δ
40	(KBr) 2924, 2852, 2804, 1580, 1440, 1400, 1290, 1270, 1120, 750, 732,	1.10-2.50(6H, m), 2.56-3.53(2H, m), 3.70-3.97(2H, m), 4.00-4.36(2H, m), 4.59(2H, s), 4.98-5.21(1H, m), 6.70(1H, d, J =6Hz), 6.97-7.63(9H, m), 8.24(1H, d, J=6Hz)
41	(KBr) 3056, 2924, 2852, 1598, 1578, 1496, 1470, 1436, 1402, 1288, 1266, 1242, 1172, 1090, 1056, 740, 690,	1.50-2.50(6H, m), 2.60-3.40(2H, m), 4.33(4H, s), 5.00-5.21(1H, m), 6.66-7.81(9H, m), 8.26(1H, d, J=6Hz)
42	(KBr) 2920, 2852, 1576, 1470, 1436, 1404, 1348, 1286, 1266, 1232, 1134, 1088, 1048, 760, 740,	1.35-2.40(6H, m), 2.55-3.41(2H, m), 3.86-4.05(2H, m), 4.15-4.36(2H, m), 4.69(2H, s), 4.96-5.21(1H, m), 6.70 (1H, d, J=6Hz), 6.93-7.76(7H, m), 8.23(1H, d, J=6Hz), 8.49(1H, d, J=4Hz)
43	(KBr) 2932, 1676, 1580, 1460, 1438, 1290, 1268, 1232, 1092, 908, 732, 648,	1.10-3.21(12H, m), 3.50(2H, t, J=7Hz), (2H, t, J=6Hz), 3.98-4.23(2H, m), 5.01-5.24 (1H, m), 6.66(1H, d, J=7Hz), 7.00-7.30 (2H, m), 7.30-7.75(2H, m), 8.23(1H, d, J=7Hz)
44	(KBr) 3064, 2932, 2856, 1490, 1440, 1406, 1346, 1288, 1262, 1226, 1200, 1134, 1108, 1062, 958, 836, 804,	1.20-2.60(8H, m), 2.27(3H, s), 2.67-3.25 (2H, m), 4.14(2H, t, J=14Hz), 5.00-5.20 (1H, m), 5.35-7.50(5H, m), 8.19(1H, s)
45	(KBr) 2924, 2848, 1468, 1450, 1432, 1394, 1342, 1260, 1232, 1198, 1152, 1054, 1030, 1006,	1.40-2.46(6H, m), 2.23(3H, s), 2.65-3.35 (2H, m), 3.69(3H, s), 3.79(3H, s), 4.93- 5.13(1H, m), 6.63-7.65(2H, m), 8.14(1H, s)
46	(neat) 2980, 2924, 2856, 1736, 1580, 1448, 1372, 1334, 1274, 1240, 1198, 1132, 1090, 1060, 806, 754, 600,	1.65-2.43(6H, m), 2.40(3H, s), 2.63-3.25 (2H, m), 3.46(3H, s), 3.63-3.83(2H, m), 3.99-4.24(2H, m), 4.96-5.16(1H, m), 6.68 (1H, d, J=7Hz), 6.91(1H, d, J=11Hz), 7.07- 7.47(2H, m), 8.22(1H, d, J=7Hz)

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Table-4 (5) a

Example No.	R	R ¹	R ²	R ³	A	Melting point (yield)
47	3-CH ₃	4-OCH ₂ CF ₂ CF ₂ H	5-OCH ₃	H	CH	Yellow amorphous powder (58.1 %) ---
48	H	OCH ₂ CH ₂ OCH ₃	H	COOCH ₂ CH ₂ OCH ₃	CH	Colorless needle crystal (79.0 %) 130-131 °C
49	3-CH ₃	OCH ₂ CH ₂ OCH ₃	H	H	CH	Colorless amorphous powder (43.9 %) ---
50	3-CH ₃	OCH ₂ CH ₂ OCH ₃	5-F	H	CH	Colorless amorphous Powder (31.3 %) ---
51	3-CH ₃	OCH ₃	5-F	H	CH	Colorless amorphous powder (65.1 %) ---
52	H	OCH ₃	H	CH ₂ COOEt	CH	Colorless powder (66.8 %) 162-163.5 °C
53	3-CH ₃	OCH ₃	H	H	CH	Colorless powder (57.4 %) 196-196.5 °C

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Table-4 (5) b

Example No.	IR [cm^{-1}]	NMR (CDCl ₃) δ
47	(KBr) 2928, 1452, 1400, 1344, 1226, 1198, 1154, 1100, 1026, 834, 806, 754,	1.40-2.38(6H,m), 2.26(3H,s), 2.86-3.15 (2H,m), 3.80(3H,s), 4.12(2H,t,J=12Hz), 5.00-5.20(1H,m), 5.10, 6.03, 6.62(1H,t, x3, J=4Hz), 6.75-7.35(3H,m), 8.18(1H,s)
48	(KBr) 2928, 1744, 1574, 1452, 1382, 1324, 1300, 1282, 1120, 1078, 758,	1.20-2.97(8H,m), 3.44(6H,s), 3.63-3.91 (4H,m), 4.03-4.23(2H,m), 4.50-4.73(2H,m), 5.68(1H,d,J=7Hz), 6.66(1H,d,J=6Hz), 7.07- 7.33(2H,m), 7.46-7.70(1H,m), 7.76-7.96 (1H,m), 8.21(1H,d,J=6Hz)
49	(KBr) 2920, 1440, 1401, 1269, 1058, 748,	1.30-1.65(7H,m), 3.49(3H,s), 2.93-3.60 (1H,m), 3.86(3H,s), 3.95-4.15(2H,d,J=7 Hz), 4.20-4.40(2H,d,J=7Hz), 5.52-6.70 (1H,m), 7.70-8.43(4H,m), 8.95(1H,s)
50	(KBr) 2920, 1438, 1401, 1340, 1259, 1129, 1051, 959	1.50-2.35(7H,m), 2.26(3H,s), 2.70-3.22 (1H,m), 3.42(3H,s), 3.55-3.80(2H,d,J=6 Hz), 3.80-4.00(2H,d,J=6Hz), 4.97-5.20 (1H,m), 6.69-7.52(3H,m), 8.15(1H,s)
51	(KBr) 2926, 2854, 1470, 1437, 1404, 1347, 1260, 1134, 750,	1.25-2.50(6H,m), 2.26(3H,s), 2.63-3.36 (2H,m), 4.72(3H,s), 5.00-5.16(1H,m), 6.74-7.50(3H,m), 8.15(1H,s)
52	(KBr) 2976, 2924, 1736, 1578, 1474, 1460, 1440, 1330, 1310, 1282, 1244, 1210, 1054, 1024,	1.23(3H,t,J=9Hz), 1.56-2.76(7H,m), 3.10-3.48(1H,m), 3.82(3H,s), 4.17(2H,q, J=9Hz), 4.92(2H,s), 5.62(1H,d,J=12Hz), 6.66(1H,d,J=7.5Hz), 7.07-7.83(4H,m), 8.22(1H,d,J=7.5Hz)
53	(KBr) 3432, 2928, 2856, 1468, 1440, 1398, 1270,	1.30-2.42(7H,m), 2.23(3H,s), 2.73-3.15 (1H,m), 3.70(3H,s), 5.01-5.16(1H,m), 6.96-7.71(4H,m), 8.15(1H,s)

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Table-4 (6) a

Example No.	R	R ¹	R ²	R ³	A	Melting point (yield)
54	H	OCH ₃	5-CH ₃	H	CH	Colorless amorphous powder (74.0 %) 94-95 °C
55	3-CH ₃	SCH ₂ CH ₂ CH ₃	H	H	CH	Colorless powder (62.4 %) 182-183 °C
56	H	OCH ₂ CH ₂ OCH ₃	H	H	N	Colorless amorphous powder (26.3 %) ---
57	H	OCH ₃	H	H	N	Colorless amorphous powder (25.8 %) ---
58	3-CH ₃	H	H	H	N	Colorless amorphous powder (21.0 %) ---
59	3-CH ₃	OCH ₃	H	H	N	Colorless powder (46.1 %) ---
60	3-CH ₃	OCH ₂ CF ₂ CF ₂ H	H	H	N	Colorless amorphous powder (53.5 %) ---

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Table-4 (6)b

Example No.	IRVcm ⁻¹	NMR(CDCl ₃) ^δ
54	(KBr) 2920, 2848, 1578, 1470, 1437, 1275, 1230, 1050, 801,	1.39-3.40(8H,m), 1.42(3H,s), 3.83(3H,s), 5.00-5.17(1H,t,J=5Hz), 6.63-6.77(1H,d,J =7Hz), 6.86-7.03(1H,d,J=10Hz), 7.10-7.53 (2H,m), 8.03-8.18(1H,d,J=6Hz)
55	(KBr) 2962, 2920, 2848, 1440, 1401, 1377, 1350, 1269, 1236, 744,	0.87-1.13(3H,t,J=7Hz), 1.12-2.40(8H,m), 2.49(3H,s), 2.50-2.76(2H,t,J=7Hz), 3.00- 3.79(2H,m), 5.06-5.28(1H,m), 7.00-7.27 (2H,m), 7.35-7.60(1H,m), 8.21(1H,s),
56	(KBr) 2921, 1578, 1450, 1396, 1269, 1232, 1122, 1057,	1.44-3.22(8H,m), 3.41(3H,s), 3.63-3.85 (2H,m), 4.00-4.22(2H,m), 5.08-5.25(1H,m), 6.65-6.77(1H,d,J=7Hz), 6.96-7.18(1H,m), 7.68-8.89(1H,m), 8.10-8.38(2H,m)
57	(KBr) 2950, 1590, 1468, 1408, 1293, 1065, 759,	1.30-3.16(8H,m), 3.83(3H,s), 5.09-5.28 (1H,m), 6.60-6.77(1H,m), 6.96-7.18(1H,m), 7.56-7.86(1H,m), 8.08-8.37(2H,m),
58	(KBr) 2930, 1470, 1401, 1060, 799,	1.44-3.30(8H,m), 2.28(3H,s), 5.10-5.31 (1H,m), 6.92-7.35(2H,m), 7.70-7.93 (1H,d,J=10Hz), 8.05-8.38(2H,s),
59	(KBr) 2930, 1590, 1470, 1070, 810,	1.30-3.42(8H,m), 2.24(3H,s), 3.72(3H,s), 5.06-5.20(1H,m), 6.98-7.20(1H,m), 7.69-7.86(1H,d,J=10Hz), 8.20(2H,s)
60	(KBr) 2925, 1456, 1397, 1272, 1011, 957, 779,	1.60-2.30(5H,m), 2.26(3H,s), 2.87-3.21 (3H,m), 3.95-4.32(3H,t,J=12Hz), 5.17-5.39 (1H,m), 5.38-6.71(2H,m), 6.96-7.23(1H,m), 7.72-7.91(1H,d,J=9Hz), 8.15-8.31(2H,s)

Example 61

9-(5-Methoxybenzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine

5 940 mg (2.64 mmol) of 9-(5-methoxybenzimidazole-2-yl)thio-4-methoxy-2,3-cycloheptenopyridine is dissolved in 48 ml of dry methylene chloride, 456 mg (2.64 mmol) of m-chloroperbenzoic acid is added portion-wise with stirring at -18 °C, and the mixture is stirred for 20 minutes. After the reaction, a saturated aqueous sodium hydrogen carbonate solution is added, followed by extraction with methylene chloride. The methylene chloride layer is washed with saturated saline and dried over anhydrous magnesium sulfate, and
10 the solvent is distilled away under reduced pressure. The resulting crystalline residue is recrystallized from chloroform-ether to obtain 564 mg (57.4 %) of 9-(5-methoxybenzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine as yellowish powder having a melting point of 145 to 148 °C.
IR_{max}(KBr): 2936, 1580, 1476, 1436, 1286, 1008 cm⁻¹.
NMR(CDCl₃)δ: 0.98-2.43(7H,m), 2.83-3.33 (1H,m), 3.78(6H,s), 4.79-5.05(1H,m), 6.68(1H,d,J = 6Hz), 6.84-
15 (1H,d,J = 8Hz), 7.00-7.87 (2H,m), 8.30(1H,d,J = 6Hz).

Example 62

4-Ethoxy-9-(5-methoxybenzimidazole-2-yl)sulfinyl-3-methyl-2,3-cycloheptenopyridine

20 In a stream of argon, 794 mg (2.07 mmol) of 4-ethoxy-9-(5-methoxybenzimidazole-2-yl)thio-3-methyl-2,3-cycloheptenopyridine is dissolved in 25 ml of methylene chloride, 424 mg (1.97 mmol) of m-chloroperbenzoic acid dissolved in 13 ml of methylene chloride is added dropwise thereto with stirring at -12 °C, and the mixture is stirred at the temperature for 5 minutes. After completion of the reaction, the
25 reaction mixture is poured into a saturated sodium hydrogen carbonate solution, followed by extraction with methylene chloride. The methylene chloride layer is washed with water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is crystallized from methylene chloride-ether to obtain 427 mg (51.6 %) of 4-ethoxy-9-(5-methoxybenzimidazole-2-yl)sulfinyl-3-methyl-2,3-cycloheptenopyridine as palely yellow powder having a melting
30 point of 152 to 154 °C.
IR_{max}(KBr): 2976, 2932, 1626, 1462, 1442, 1404, 1204, 1184, 1154, 1054, 1024, 998, 962, 818, 808 cm⁻¹.
NMR(CDCl₃)δ: 1.00-2.65(8H,m), 1.31(3H,t,J = 7Hz), 2.19(3H,s), 2.73-3.66 (2H,m), 3.82(3H,s), 4.86-5.23 (1H,m), 6.55(1H,bs), 6.85(1H, bd,J = 9Hz), 7.62(1H,bd,J = 9Hz), 8.20(1H,bs).

Example 63

9-[1-(Benzoyloxycarbonyl)benzimidazole-2-yl]sulfinyl-4-methoxy-2,3-cycloheptenopyridine

40 In a stream of argon, 630 mg (1.37 mmol) of 9-[1-(benzoyloxycarbonyl)benzimidazole-2-yl]thio-4-methoxy-2,3-cycloheptenopyridine is dissolved in 20 ml of methylene chloride, and under stirring at -20 °C to -10 °C, 281 mg (1.30 mmol) of m-chloroperbenzoic acid dissolved in 10 ml of methylene chloride is dropwise added little by little. After stirring at -10 °C to 0 °C for 50 minutes, the reaction mixture is poured into a saturated aqueous sodium hydrogen carbonate solution, followed by extraction with methylene
45 chloride. The methylene chloride layer is washed with water and saturated saline ad dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The residue is crystallized from methylene chloride-ether-hexane and further recrystallized from methylene chlordie-ether to obtain 171 mg (27.9 %) of 9-[1-(benzoyloxycarbonyl)benzimidazole-2-yl]sulfinyl-4-methoxy-2,3-cycloheptenopyridine as colorless powder having a melting point of 91 to 95 °C.
50 IR_{max}(KBr): 2928, 2852, 1752, 1734, 1580, 1474, 1440, 1396, 1332, 1304, 1284, 1256, 1204, 1118, 1074 cm⁻¹.
NMR(CDCl₃)δ: 1.62-2.67(7H,m), 3.06-3.45 (1H,m), 3.77(3H,s), 4.85(1H,d,J = 10.5Hz), 5.43(2H,s), 6.55 (1H,d,J = 7.5Hz), 7.06-7.53(6H,m), 7.56-8.06(2H,m), 7.99(1H,d,J = 7.5Hz).

Example 64

9-[1-(t-Butoxycarbonylmethoxymethyl)benzimidazole-2-yl]sulfinyl-4-methoxy-2,3-cycloheptenopyridine

5 In a stream of argon, 469 mg (1.00 mmol) of 9-[1-(t-butoxycarbonylmethoxymethyl)benzimidazole-2-yl]-thio-4-methoxy-2,3-cycloheptenopyridine is dissolved in 20 ml of methylene chloride, 205 mg (0.95 mmol) of m-chloroperbenzoic acid dissolved in 10 ml of methylene chloride is added dropwise little by little under stirring at -20 °C to -10 °C, and the mixture is stirred at that temperature for 1 hour. The reaction mixture is poured into a saturated aqueous sodium hydrogen carbonate solution, followed by extraction with 10 methylene chloride. The methylene chloride layer is washed with water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The residue is purified by activated alumina column chromatography (ethyl acetate-hexane 1:2 → 1:1 → ethyl acetate) to obtain 165 mg (35.2 %) of 9-[1-(t-butoxycarbonylmethoxymethyl)benzimidazole-2-yl]sulfinyl-4-methoxy-2,3-cycloheptenopyridine.

15 IR_{max}(KBr): 2976, 2932, 1742, 1580, 1474, 1450, 1368, 1284, 1238, 1156, 1054 cm⁻¹.

NMR(CDCl₃) δ : 1.45(9H,s), 1.63-2.76(7H,m), 3.06-3.42(1H,m), 3.81(3H,s), 4.97(1H,d,J = 9.0Hz), 5.13-7.5Hz), 5.67(1H,d,J = 13.5Hz), 5.91(1H,d,J = 13.5Hz), 6.65(1H,d,J = 7.5Hz), 7.04-7.90(4H,m), 8.22(1H,d,J = 7.5Hz).

Example 65

9-[1-(Ethoxycarbonyl)benzimidazole-2-yl]sulfinyl-4-methoxy-2,3-cycloheptenopyridine

20 In a stream of argon, 227 mg (0.62 mmol) of 9-(benzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine sodium salt is dissolved in 15 ml of dry THF, 0.09 ml (0.93 mmol) of ethyl chlorocarbonate is added dropwise under stirring at room temperature, and the mixture is stirred for 1 hour. After the reaction, the solvent is distilled away under reduced pressure, the residue is dissolved in methylene chloride, and the solution is washed with water. The methylene chloride layer is dried over anhydrous magnesium sulfate, the solvent is distilled away under reduced pressure, and the solid residue is recrystallized from methylene 25 chlordie-ether to obtain 194 mg (75.2 %) of 9[(1-ethoxycarbonyl)benzimidazole-2-yl]sulfinyl-4-methoxy-2,3-cycloheptenopyridine as colorless powder having a melting point of 183 to 185 °C.

IR_{max}(KBr): 2924, 1756, 1578, 1472, 1450, 1428, 1400, 1376, 1342, 1316, 1296, 1282, 1260, 1186, 1020, 756, 738 cm⁻¹.

30 NMR(CDCl₃) δ : 1.08-2.73(7H,m), 1.43(3H,t,J = 7Hz), 3.13-3.50(1H,m), 3.78 (3H,s), 4.53(2H,q,J = 7Hz), 4.93 (1H,d,J = 9Hz), 6.58(1H,d,J = 5Hz), 7.20-7.53(2H,m), 7.81-8.02 (2H,m), 8.08(1H,d,J = 5Hz).

Example 66

9-(Benzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine sodium salt

40 In a stream of argon, 100g (527 mmol) of 28 % sodium methylate and 530 ml of dry methylene chloride are placed in a 5 l three-necked flask, and under stirring at room temperature, 120 g (350 mmol) of 9-(benzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine is added, and the mixture is stirred for 2 hours.

45 Then, ether is added dropwise, and after 30 minutes stirring at room tempearture, the mixture is stirred at -30 °C for 2 hours. The deposited crystals are collected by filtration, and after removal of the methanol insoluble matters and acetone insoluble matters, recrysatlized from methylene chloride-ether to obtain 107 g (83.9 %) of 9-(benzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine sodium salt as colorless powder having a melting point of 167 to 175 °C (decomposition).

50 IR_{max}(KBr): 3372, 3048, 2972, 2928, 2856, 1580, 1474, 1298, 1270, 1090, 1052, 1036, 820, 800, 744 cm⁻¹.

NMR(CDCl₃-DMSO-d₆) δ : 1.00-2.63(7H,m), 2.95-3.34(1H,m), 3.82(3H,s), 4.75(1H,d,J = 6Hz), 6.65-(1H,d,J = 5Hz), 6.85-7.10(2H,m), 7.40-7.65 (2H,m), 8.23(1H,d,J = 5Hz).

Example 67

9-(Benzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine potassium salt

5 In a stream of argon, 342 mg (1.00 mmol) of 9-(benzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine is dissolved in 5 ml of dry methylene chloride, 137 mg (1.20 mmol) of potassium t-butoxide is added, and the mixture is stirred at room temperature for 16.5 hours.

10 Then, ether is added dropwise, followed by stirring at room temperature for 2 hours. The deposited crystals are collected by filtration, and recrystallized from chloroform and then from methanol-ether to obtain 110 mg (28.9 %) of 9-(benzimidazole-2-yl)sulfinyl-4-methoxy-2,3-cycloheptenopyridine potassium salt as colorless powder having a melting point of 159 to 163 °C (decomposition).

IR_vmax(KBr): 3400, 2924, 1580, 1476, 1460, 1428, 1376, 1308, 1288, 1264, 1082, 1058, 1030, 802, 742 cm⁻¹.

NMR(CDCl₃-DMSO-d₆)_δ: 1.00-2.73(7H,m), 3.00-3.45(1H,m), 3.79(3H,s), 4.81(1H,bs), 6.52(1H,d,J=5Hz), 15 6.77-7.06(2H,m), 7.32-7.63(2H,m), (2H,m), 8.13(1H,d,J=5Hz).

Example 68

9-[pyrido[2,3-d]imidazole-2-yl]sulfinyl-2,3-cycloheptenopyridine

20 In a stream of argon, 700g (2.36 mmol) of 9-[pyrido[2,3-d]imidazole-2-yl]thio-2,3-cycloheptenopyridine is dissolved in 25 ml of methylene chloride, 358 mg (2.25 mmol) of m-chloroperbenzoic acid dissolved in 4 ml of methylene chloride is added dropwise with stirring at -18 °C, and the mixture is stirred at the same temperature for 5 minutes. After completion of the reaction, the reaction mixture is poured into a saturated aqueous sodium hydrogen carbonate solution and extracted with methylene chloride. The methylene chloride layer is washed with water and saturated saline and dried over anhydrous magnesium sulfate, and the solvent is distilled away under reduced pressure. The resulting residue is crystallized from methylene chloride-ether to obtain 252 mg (34.2 %) of 9-[pyrido[2,3-d]imidazole-2-yl]sulfinyl-2,3-cycloheptenopyridine as colorless crystals having a melting point of 133.5 to 135 °C.

30 IR_vmax(KBr): 2960, 1635, 1455, 1295, 1064, 821 cm⁻¹.

NMR(CDCl₃) : 1.10-2.28(5H,m), 2.28-3.20 (3H,m), 4.56-4.86(1H,m), 6.83-7.60(3H,m), 7.90-8.40(2H,m), 8.70-8.40(1H,m).

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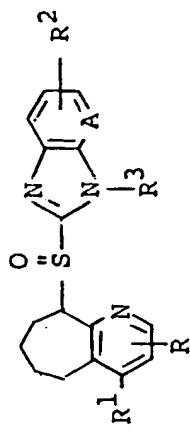
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The compounds shown in Table-5 are obtained in the same manner as in Examples 61 to 68.

Table-5 (1) a



Example No.	R	R ¹	R ²	R ³	Melting Point (yield)
69	H	H	5-OCH ₃	H	Colorless powder (55.7 %) 132-134 C
70	H	H	5-NO ₂	H	Yellow powder (48.8 %) 129-134 C
71	H	H	5-Cl	H	Yellowish amorphous powder (40.0 %) ---
72	H	H	5-F	H	Colorless powder (33.0 %) 155-156 C
73	H	H	5-CH ₃	H	Yellowish amorphous powder (64.8 %) ---

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Table-5 (1)b

Example No.	IR ν cm $^{-1}$	NMR (CDCl $_3$) δ
	(KBr) 3116, 3092, 2940, 1626, 1454, 1438 1198, 1026, 820,	1.15-2.33 (6H, m), 2.53-2.84 (2H, m), 3.79 (3H, s), 4.84-5.08 (1H, m), 6.47-7.78 (5H, m), 8.35 (1H, d, J=5Hz)
69	(KBr) 2935, 2858, 1620, 1522, 1434, 1342, 1040, 812, 738,	0.73-3.18 (8H, m), 4.73-5.18 (1H, m), 6.94-7.73 (3H, m), 7.96-8.57 (3H, m)
	(KBr) 3072, 2932, 2852, 1615, 1578, 1454, 1434, 1042, 920, 806,	1.03-2.46 (6H, m), 2.62-2.93 (2H, m), 4.70-5.04 (1H, m), 6.86-7.87 (5H, m), 8.31 (1H, d, J=5Hz)
71	(KBr) 3064, 2858, 1626, 1578, 1490, 1454, 1434, 1348, 1108, 1028, 968, 802, 748,	1.13-2.40 (6H, m), 2.45-3.09 (2H, m), 4.85-5.13 (1H, m), 6.68-7.90 (5H, m), 8.35 (1H, d, J=6Hz)
	(KBr) 3056, 2982, 2856, 1578, 1454, 1434, 1038, 968, 804, 754,	1.23-2.15 (6H, m), 2.40 (3H, s), 2.43-2.96 (2H, m), 4.83-5.18 (1H, m), 6.78-7.83 (5H, m), 8.34 (1H, d, J=5Hz)
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Table-5 (2) a

Example No.	R	R ¹	R ²	R ³	A	Melting Point (yield)
74	H	H	5-CF ₃	H	CH	Palely yellow amorphous powder (34.4 %) ---
75	H	OCH ₃	H	H	CH	Yellowish powder (63.5 %) 147-150 °C
76	H	OCH ₃	5-F	H	CH	Colorless powder (46.3 %) 161-163 °C
77	H	OEt	H	H	CH	Palely brown powder (52.4 %) 112-118 °C (decomposed)
78	H	n-O-Bu	H	H	CH	Colorless needle crystal (58.0 %) 150-154 °C (decomposed)
79	H		H	H	CH	Colorless prismatic crystal (66.2 %) 162-165 °C
80	H			H	CH	Palely brown prismatic crystal (59.8 %) 138-140 °C (decomposed)

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Table-5 (2) b

Example No.	IR ν cm ⁻¹	NMR (CDCl ₃) δ
74	(KBr) 2932, 2856, 1434, 1330, 1162, 1120, 1048, 814,	1.13-2.35 (6H, m), 2.46-3.03 (2H, m), 4.83-5.21 (1H, m), 6.90-8.10 (5H, m), 8.27 (1H, d, J=5Hz)
75	(KBr) 3068, 2972, 2932, 2852, 1580, 1476, 1454, 1430, 1286, 1270, 1086, 1054, 996, 746,	1.07-2.74 (6H, m), 2.95-3.40 (2H, m), 3.82 (3H, s), 4.73-4.98 (1H, m), 6.69 (1H, d, J=6 Hz), 7.06-7.92 (4H, m), 8.30 (1H, d, J=6Hz)
76	(KBr) 3068, 2976, 2940, 2856, 1620, 1580, 1476, 1430, 1284, 1276, 1088, 1058, 994, 812,	1.00-2.55 (6H, m), 2.92-3.30 (2H, m), 3.79 (3H, s), 4.73-5.05 (1H, m), 6.68 (1H, d, J=5 Hz), 6.77-7.76 (3H, m), 8.28 (1H, d, J=5Hz)
77	(KBr) 3430, 3064, 2976, 2928, 1580, 1466, 1430, 1312, 1286, 1268, 1052, 744,	1.43 (3H, t, J=7.5Hz), 1.60-2.65 (7H, m), 3.03-3.36 (1H, m), 4.03 (2H, q, J=7.5Hz), 4.93 (1H, d, J=6Hz), 6.65 (1H, d, J=7.5Hz), 7.09-7.70 (4H, m), 8.26 (1H, d, J=7.5Hz)
78	(KBr) 3450, 3056, 2960, 2936, 1588, 1466, 1428, 1310, 1290, 1268, 1046,	0.96 (3H, t, J=7.5Hz), 1.13-2.56 (11H, m), 3.05-3.34 (1H, m), 3.95 (2H, t, J=7.5Hz), 4.80 (1H, d, J=9Hz), 6.67 (1H, d, J=7.5Hz), 7.10-7.93 (4H, m), 8.26 (1H, d, J=7.5Hz),
79	(KBr) 3500, 3040, 2936, 2856, 1576, 1506, 1466, 1428, 1268, 1242, 1206, 1008,	1.12-2.70 (7H, m), 2.33 (3H, s), 3.10-3.53 (1H, m), 4.89 (1H, d, J=7.5Hz), 6.50 (1H, d, J=7.5Hz), 6.76 (2H, d, J=10.5Hz), 6.96-7.93 (4H, m), 7.16 (2H, d, J=10.5Hz), 8.20 (1H, d, J=10.5Hz)
80	(KBr) 3456, 3012, 2944, 2872, 2808, 1580, 1472, 1452, 1428, 1412, 1298, 1266, 1038, 1008,	0.20-0.76 (4H, m), 1.05-2.66 (8H, m), 3.10 -3.52 (1H, m), 3.12 (2H, d, J=7.5Hz), 4.75 (1H, d, J=10.5Hz), 6.65 (1H, d, J=7.5Hz) 7.06-7.95 (4H, m), 8.25 (1H, d, J=7.5Hz)

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Table-5 (3) a

Example No.	R	R ¹	R ²	R ³	A	Melting Point (yield)
81	H		H	H	CH	Colorless powder (55.2 %) 147-148 °C (decomposed)
82	H	OCH ₃	H	CH ₃ COCH ₃	CH	Colorless powder (10.5 %) 141-144 °C
83	H	OCH ₃	H	CH ₂ OCH ₃	CH	Colorless powder (25.9 %) 132-136 °C
84	H	OCH ₃	H	CH ₂ OEt	CH	Colorless powder (51.8 %) 112-114 °C
85	H	OCH ₃	H	CH ₂ O(CH ₂) ₂ OCH ₃	CH	Colorless amorphous powder (47.7 %) 45-49 °C
86	H	OCH ₃	H	COO(CH ₂) ₂ OCH ₃	CH	Colorless powder (35.7 %) 176-179 °C
87	H	OCH ₃	H	CH ₂ COOEt	CH	Colorless powder (24.2 %) ---

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Table-5 (3)b

Example No.	IR ν cm $^{-1}$	NMR (CDCl ₃) δ
81	(KBr) 3432, 3068, 2972, 2932, 1578, 1464, 1432, 1290, 1268, 1052, 1006,	1.13-2.63(7H,m), 3.10-3.48(1H,m), 3.68-4.43(5H,m), 4.75(1H,d,J=10.5Hz), 6.73(1H,d,J=7.5Hz), 8.20(1H,d,J=7.5Hz)
82	(KBr) 2932, 1752, 1580, 1440, 1364, 1350, 1284, 1252, 1206, 1088, 1050, 1024,	1.23-2.81(7H,m), 2.10(3H,s), 3.06-3.46 (1H,m), 3.81(3H,s), 5.11(1H,d,J=9Hz), 6.46, 6.76(1Hx2,d,J=13.5Hz), 6.63(1H,d, J=7.5Hz), 7.10-7.93(4H,m), 8.15(1H,d, J=7.5Hz)
83	(KBr) 2920, 1580, 1476, 1434, 1334, 1318, 1286, 1262, 1110, 1092, 1044,	1.23-2.80(7H,m), 3.10-3.53(1H,m), 3.41(3H,s), 3.82(3H,s), 5.02-5.29 (1H,m), 5.75, 6.06(1Hx2,d,J=13.5Hz), 6.65(1H,d,J=7.5Hz), 7.13-7.93(4H,m), 8.16(1H,d,J=7.5Hz)
84	(KBr) 2928, 2852, 1580, 1474, 1438, 1340, 1092, 1052,	1.19(3H,t,J=9Hz), 1.48-2.83(7H,m), 3.08-3.43(1H,m), 3.62(2H,q,J=9Hz), 3.80(3H,s), 5.03-5.33(1H,m), 5.76, 5.98 (1Hx2,d,J=13.5Hz), 6.65(1H,d,J=7.5Hz), 7.14-7.90(4H,m), 8.16(1H,d,J=7.5Hz)
85	(KBr) 2924, 2852, 1588, 1464, 1438, 1336, 1316, 1284, 1134, 1090,	1.34-2.80(8H,m), 3.30(3H,s), 3.47(2H, t,J=6Hz), 3.73(2H,t,J=6Hz), 3.80(3H, s), 5.12(1H,d,J=9Hz), 5.84, 6.13(1Hx2, d,J=13.5Hz), 6.65(1H,d,J=7.5Hz), 7.13- 7.92(4H,m), 8.13(1H,d,J=7.5Hz)
86	(KBr) 2920, 1746, 1580, 1474, 1448, 1380, 1330, 1284, 1256, 1206, 1078,	1.53-2.75(8H,m), 3.33(3H,s), 3.66(2H, t,J=6Hz), 3.76(3H,s), 4.57(2H,t,J=6Hz) 4.89(1H,d,J=1.2Hz), 6.56(1H,d,J=7.5Hz), 7.08-8.15(4H,m), 8.09(1H,d,J=7.5Hz)
87	(KBr) 2932, 2852, 1744, 1580, 1476, 1448, 1308, 1222, 1048,	1.26(3H,t,J=9Hz), 1.60-2.76(7H,m), 3.06-3.37(1H,m), 3.81(3H,s), 4.23(2H, q,J=9Hz), 4.94-5.17(1H,m), 5.13, 5.78 (1Hx2,d,J=22.5Hz), 6.65(1H,d,J=7.5Hz), 7.04-7.86(4H,m), 8.20(1H,d,J=7.5Hz)

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Table-5 (4) a

Example No.	R	R ¹	R ²	R ³	A	Melting point (yield)
88	3-CH ₃	OCH ₃	H	H	CH	Colorless powder (64.2 %) 166-168 °C (decomposed)
89	3-CH ₃	OCH ₃	H	Na ⁺	CH	Colorless powder (67.7 %) 189-195 °C (decomposed)
90	H	OCH ₂ CH ₂ OCH ₃	F	H	CH	Colorless powder (51.7 %) 141-143 °C
91	H	OCH ₃	5,6-OCH ₃	H	CH	Colorless powder (71.8 %) 176-178 °C (decomposed)
92	H	OCH ₂ CF ₃	H	H	CH	Colorless powder (39.2 %) ---
93	H	OCH ₂ CH=CH ₂	H	H	CH	Yellow amorphous powder (37.7 %) ---
94	H	OCH ₂ CH ₂ OCH ₃	H	H	CH	Colorless powder (42.0 %) ---

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Table-5 (4)b

Example No.	IRνcm ⁻¹	NMR (CDCl ₃) ^d
88	(KBr) 3448, 3070, 2932, 1470, 1455, 1434, 1398, 1266, 1056, 1011,	1.38-2.70(7H,m), 2.23(3H,s), 2.87-3.26 (1H,m), 3.55(3H,s), 4.86(1H,d,J=9Hz), 7.03-7.84(4H,m), 8.20(1H,s)
89	(KBr) 3432, 2932, 1562, 1450, 1380, 1290, 1270, 1056, 1006, 1064, 1036, 1016, 994, 966, 836, 806, 796,	*1 1.33-2.26(7H,m), 2.10(3H,s), 2.84-3.25 (1H,m), 3.63(3H,s), 4.60-4.85(1H,m), 6.76-7.10(2H,m), 7.30-7.63(2H,m), 8.02(1H,s)
90	(KBr) 3036, 2988, 2936, 2880, 2788, 1576, 1476, 1448, 1430, 1406, 1276, 1132, 1106, 1086, 1064, 1036, 1016, 994, 966, 836, 806, 796,	1.00-2.65(7H,m), 2.97-3.30(1H,m), 3.39 (3H,s), 3.58-3.81(2H,m), 3.93-4.21(3H, m), 4.70-5.01(1H,m), 6.69(1H,d,J=6Hz), 6.70-7.80(3H,m), 8.24(1H,d,J=6Hz)
91	(KBr) 3064, 2976, 2932, 2856, 1580, 1490, 1478, 1434, 1326, 1284, 1240, 1194, 1180, 1140, 1054, 1008, 998, 830,	1.00-3.30(8H,m), 3.80(3H,s), 3.87(6H, s), 4.85-5.12(1H,m), 6.65-6.80(2H,d,J= 6Hz), 7.06-7.30(1H,m), 8.29(1H,d,J= 6Hz)
92	(KBr) 3432, 3304, 2932, 1580, 1472, 1454, 1436, 1370, 1318, 1294, 1266, 1160, 1142, 1102, 1044, 976,	*2 1.36-3.40(8H,m), 4.47(2H,m), 4.73-4.95 (1H,m), 6.77(1H,d,J=6Hz), 7.16-7.37 (2H,m), 7.53-7.81(2H,m), 8.44(1H,d,J= 6Hz)
93	(KBr) 2952, 2920, 2872, 1580, 1472, 1426, 1310, 1298, 1282, 1040, 1014, 994, 750, 746,	1.00-3.33(8H,m), 4.35-4.63(2H,m), 4.67-5.00(1H,m), 5.07-5.56(2H,m), 5.70 -6.20(1H,m), 6.57(1H,d,J=7Hz), 6.92- 7.33(2H,m), 7.36-8.07(3H,m), 8.18(1H, d,J=7Hz)
94	(KBr) 2924, 2876, 2852, 1580, 1472, 1452, 1428, 1270, 1082, 1052, 998, 750,	1.00-2.70(8H,m), 3.39(3H,s), 3.60-3.82 (2H,m), 3.95-4.21(2H,m), 4.78-5.03 (1H,m), 6.66(1H,d,J=6Hz), 7.07-7.34 (2H,m), 7.36-7.67(2H,m), 8.24(1H,d,J= 6Hz)

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Table-5 (5) a

Example No.	R	R ¹	R ²	R ³	A	Melting point (yield)
95	H	OCH ₂ CH ₂ OH	H	H	CH	Yellow amorphous powder (24.3 %)
96	H	OCH ₂ CH ₂ OOCCH ₃	H	H	CH	Paley orange powder (34.3 %) 135-137 °C
97	H	O(CH ₂) ₃ OCH ₃	H	H	CH	Colorless powder (28.4 %) 135-136.5 °C
98	H	O(CH ₂) ₂ OCH ₂ Ph	H	H	CH	Yellow amorphous powder (89.3 %)
99	H	O(CH ₂) ₂ OPh	H	H	CH	Colorless powder (39.7 %) 144-145 °C
100	H	O(CH ₂) ₂ OCH ₂ Py	H	H	CH	Yellow amorphous powder (40.0 %)
101	H	O(CH ₂) ₂ N 	H	H	CH	Colorless powder (53.3 %) 140-141 °C

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Table-5 (5)b

Example No.	$\nu_{IR} \text{cm}^{-1}$	NMR (CDCl ₃) δ
95	(KBr) 3416, 2928, 2856, 1580, 1472, 1450, 1312, 1290, 1270, 1240, 1136, 1078, 1054, 946, 904, 800, 746,	1.00-3.60(8H,m), 3.80-4.33(4H,m), 4.66-5.00(1H,m), 6.68(1H,d,J=6Hz), 7.06-7.83(4H,m), 8.23(1H,d,J=6Hz)
96	(KBr) 3064, 2968, 2936, 2856, 1736, 1580, 1452, 1432, 1286, 1268, 1250, 1230, 1092, 1058, 1006, 744,	1.06-3.43(8H,m), 2.08(3H,s), 4.05-4.28 (2H,m), 4.33-4.53(2H,m), 4.69-4.96 (1H,m), 4.68(1H,d,J=5Hz), 7.10-8.00 (4H,m), 8.28(1H,d,J=5Hz)
97	(KBr) 3064, 3012, 2932, 2872, 2808, 1580, 1478, 1458, 1430, 1412, 1310, 1288, 1270, 1192, 1138, 1118, 1096, 1082, 1054, 1006, 816, 800, 750,	0.99-2.65(10H,m), 3.31(3H,s), 3.50(2H, t,J=6Hz), 4.06(2H,t,J=6Hz,6Hz), 4.63-4.93(1H,m), 6.70(1H,d,J=6Hz), 7.03-7.70(4H,m), 8.27(1H,d,J=6Hz)
98	(KBr) 3060, 2924, 2856, 1578, 1470, 1452, 1428, 1310, 1286, 1268, 1128, 1088, 1036, 1002, 800, 742, 696,	1.06-3.59(8H,m), 3.67-3.93(2H,m), 3.98- 4.25(2H,m), 4.57(2H,s), 4.66-4.99(1H, m), 6.67(1H,d,J=6Hz), 7.00-7.71(9H,m), 8.25(1H,d,J=6Hz)
99	(KBr) 3064, 2820, 1580, 1458, 1478, 1454, 1432, 1272, 1244, 1086, 1064, 1006, 814, 800, 756, 744	1.00-3.35(8H,m), 4.27(3H,s), 4.66-4.92 (1H,m), 6.67(1H,d,J=6Hz), 6.78-7.71 (9H,m), 8.22(1H,d,J=6Hz)
100	(KBr) 3060, 2928, 2856, 1578, 1474, 1450, 1432, 1356, 1286, 1268, 1238, 1134, 1088, 1046, 1002, 800, 746,	1.00-3.45(8H,m), 3.77-4.03(2H,m), 4.03-4.31(2H,m), 4.69(2H,s), 4.75-5.01 (1H,m), 6.68(1H,d,J=6Hz), 7.00-7.80 (7H,m), 8.25(1H,d,J=6Hz), 8.52(1H,d, J=6Hz)
101	(KBr) 3064, 3020, 2932, 2864, 2800, 1692, 1580, 1458, 1426, 1288, 1086, 998, 746,	1.00-2.70(12H,m), 2.93-3.80(4H,m), 3.85-4.33(2H,m), 4.65-5.00(1H,m), 6.66(1H,d,J=5Hz), 6.98-8.06(4H,m), 8.26(1H,d,J=5Hz)

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Table-5 (6) a

Example No.	R	R ¹	R ²	R ³	A	Melting point (yield)
102	H	OCH ₂ CF ₂ CFH ₂	H	Na ⁺	CH	Colorless powder (72.7 %) 169-171.5 °C
103	H	OCH ₃	H	CH ₂ OH	CH	Colorless powder (42.7 %) 120-122 °C
104	3-CH ₃	OCH ₂ CF ₂ CF ₂ H	5-F	H	CH	Colorless powder (44.8 %) 163-165 °C
105	3-CH ₃	OCH ₃	5-OCH ₃	H	CH	Colorless powder (60.4 %) 163-165 °C (decomposed)
106	H	OCH ₂ CH ₂ OCH ₃	5-CH ₃	H	CH	Palely orange powder (42.7 %) 118-121 °C
107	3-CH ₃	OCH ₂ CF ₂ CF ₂ H	5-OCH ₃	H	CH	Colorless powder (38.8 %) 166-168 °C
108	H	OCH ₃	5-CH ₃	H	CH	Colorless powder (39.5 %) 155-156 °C

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Table-5 (6) b

Example No.	IR/cm ⁻¹	NMR (CDCl ₃) δ
102	(KBr) 3388, 3052, 2932, 2860, 1580, 1472, 1454, 1378, 1292, 1270, 1248, 1202, 1122, 1020, 802, 746	*1 1.16-3.50(8H,m), 4.16-5.00(3H,m), 6.13-6.37(1H,m), 6.60-7.10(3H,m), 7.30-7.69(2H,m), 8.23(1H,d,J=6Hz)
103	(KBr) 3256, 3060, 2924, 2852, 1580, 1474, 1432, 1340, 1314, 1282, 1244, 1136, 1054, 814, 742,	1.14-3.50(8H,m), 3.84(3H,s), 5.07-5.33(1H,m), 5.66(1H,d,J=12Hz), 6.17(1H,d,J=12Hz), 6.72(1H,d,J=6Hz), 7.13-7.90(4H,m), 8.06-8.40(1H,m),
104	(KBr) 3034, 2932, 2854, 1497, 1470, 1455, 1434, 1413, 1263, 1221, 1197, 1137, 1110, 1080, 1059, 1002, 966, 954, 843, 810,	*2 1.13-3.29(8H,m), 2.21(3H,s), 3.75-4.24 (2H,m), 4.68-5.02(1H,m), 5.36-6.76 (1H,m), 6.76-7.83(3H,m), 8.17(1H,s)
105	(KBr) 3064, 3000, 2924, 2852, 1626, 1454, 1438, 1406, 1396, 1204, 1184, 1054, 1022, 1008, 996, 962, 820, 808,	1.10-3.20(8H,m), 2.17(3H,s), 3.41(3H, s), 3.80(3H,s), 4.86-5.26(1H,m), 6.51(1H,bs), 6.70-7.30(2H,m), 7.46- 7.71(1H,d,J=10Hz), 8.18(1H,s)
106	(neat) 3048, 2976, 2932, 2852, 1578, 1452, 1430, 1334, 1308, 1288, 1274, 1196, 1134, 1086, 1060, 1008, 966, 802,	1.05-3.30(8H,m), 2.44(3H,s), 3.40(3H, s), 3.55-3.85(2H,m), 3.90-4.23(2H,m), 4.60-4.96(1H,m), 6.70(1H,d,J=6Hz), 6.86-7.28(2H,m), 7.36-7.80(1H,m), 8.28(1H,d,J=6Hz)
107	(KBr) 3080, 3048, 3004, 2936, 2904, 1624, 1460, 1406, 1200, 1178, 1126, 1112, 1094, 1070, 996, 964, 816,	1.07-2.03(6H,m), 2.19(3H,s), 2.26-3.15 (2H,m), 3.40-4.02(2H,m), 3.81(3H,s), 5.03-7.30(4H,m), 7.61(1H,d,J=10Hz), 8.26(1H,s)
108	(KBr) 2974, 2926, 1581, 1479, 1452, 1434, 1284, 1086, 1053, 1008, 822,	1.20-2.70(7H,m), 2.68(3H,s), 3.21-3.69 (1H,m), 4.19(3H,s), 5.20-5.45(1H,d,J=11Hz), 7.27-7.43(1H,d,J=7Hz), 7.62- 7.90(2H,m), 8.15-8.52(1H,m), 9.06-9.18 (1H,d,J=7Hz)

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Table-5 (7)a

Example No.	R	R ¹	R ²	R ³	A	Melting Point (yield)
109	H	OCH ₂ CH ₂ OCH ₃	H	COOCH ₂ CH ₂ OCH ₃	CH	Colorless powder (16.7 %) 108-110 °C
110	H	OCH ₃	H	H	N	Colorless powder (44.0 %) 139-140 °C
111	H	OCH ₂ Ph	H	H	CH	Colorless powder (62.5 %) 155-158.5 °C (decomposed)
112	H	OCH ₂ CF ₂ CF ₃	H	H	CH	Colorless powder (60.8 %) 161-162 °C (decomposed)
113	H	OCH ₂ CF ₂ CF ₂ H	H	H	CH	Colorless powder (65.4 %) 150-154 °C (decomposed)
114	H	SCH ₂ CH ₂ CH ₃	H	H	CH	Colorless Powder (45.2 %) 133-134 °C (decomposed)
115	H		H	H	CH	Brown powder (18.4 %) 143-145 °C (decomposed)

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Table-5 (7)b

Example No.	IRνcm ⁻¹	NMR (CDCl ₃) ^f
109	(KBr) 2926, 1746, 1578, 1449, 1419, 1374, 1323, 1305, 1287, 1254, 1206, 1119, 1077, 996, 840, 756, 747,	1.10-2.66(6H,m), 3.36(3H,s), 3.40(3H, s), 3.55-3.83(4H,m), 3.96-4.20(2H,m), 4.40-4.71(2H,m), 4.91(1H,d,J=10Hz), 6.58(1H,d,J=6Hz), 7.15-7.51(2H,m), 7.66-8.03(2H,m), 8.08(1H,d,J=6Hz)
110	(KBr) 2920, 1583, 1479, 1291, 1266, 1059, 800,	1.19-2.70(7H,m), 3.12-3.50(1H,m), 3.79(3H,s), 4.56-4.80(1H,d,J=10Hz), 6.59-6.75(1H,d,J=6Hz), 7.10-7.33(1H, dd,J=6Hz), 8.00-8.36(2H,m), 8.36-8.65 (1H,d,J=5Hz)
111	(KBr) 3064, 2932, 1578, 1474, 1462, 1454, 1432, 1284, 1268, 1044, 1024, 1010, 798, 748, 424,	1.00-2.66(7H,m), 3.08-3.43(1H,m), 4.84(1H,d,J=7Hz), 5.04(2H,s), 6.73(1H, d,J=5Hz), 7.10-7.93(4H,m), 7.33(5H,s), 8.27(1H,d,J=5Hz)
112	(KBr) 3320, 2940, 1578, 1470, 1454, 1436, 1372, 1316, 1294, 1266, 1212, 1196, 1142, 1102, 1046, 946, 748,	1.04-2.66(7H,m), 2.95-3.40(1H,m), 4.38(2H,t,J=12Hz), 4.90(1H,d,J=6Hz), 6.63(1H,d,J=5Hz), 7.10-7.92(4H,m), 8.32(1H,d,J=5Hz)
113	(KBr) 3320, 2932, 1580, 1472, 1454, 1432, 1372, 1316, 1292, 1270, 1240, 1222, 1206, 1118, 1068, 1046, 946, 820, 748,	1.15-3.52(8H,m), 4.33(2H,t,J=12Hz), 4.92(1H,d,J=6Hz), 5.28,5.93,6.52(1H,t, x3,J=3Hz), 6.65(1H,d,J=6Hz), 7.10-7.90 4H,m), 8.32(1H,d,J=6Hz), 11.70(1H,br)
114	(KBr) 3068, 2960, 2928, 2868, 1564, 1452, 1432, 1406, 1266, 1024, 800, 766, 744,	1.06(3H,t,J=7Hz), 1.25-3.67(10H,m), 2.87(2H,t,J=7Hz), 4.92(1H,d,J=6Hz), 6.96(1H,d,J=5Hz), 7.05-7.97(4H,m), 8.24(1H,d,J=5Hz)
115	(KBr) 3456, 3064, 2932, 2856, 1630, 1578, 1452, 1430, 1266, 1114, 1024, 1006, 990, 744,	*2 1.10-3.40(12H,m), 3.70-4.00(4H,m), 4.63-4.85(1H,m), 6.87(1H,d,J=6Hz), 7.18-7.80(4H,m), 8.29(1H,d,J=6Hz)

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Table-5 (8)a

Example No.	R	R ¹	R ²	R ³	A	Melting point (yield)
116	H	OCH ₃	H	O CH ₂ OCPH	CH	Palely brown powder (23.7 %) 138-141 °C
117	H	C1	5-OCH ₃	H	CH	Colorless powder (44.2 %) 153-155 °C (decomposed)
118	3-CH ₃	OCH ₂ CH ₂ OCH ₃	H	H	CH	Colorless powder (77.1 %) 148-150 °C
119	3-CH ₃	OCH ₂ CH ₂ OCH ₃	5-F	H	CH	Colorless powder (69.5 %) 146-147 °C
120	3-CH ₃	OCH ₃	5-F	H	CH	Colorless powder (50.7 %) 160-161.5 °C
121	H	OCH ₂ CF ₃	H	Na	CH	Colorless powder (77.6 %) ---
122	3-CH ₃	SCH ₂ CH ₂ CH ₃	H	H	CH	Colorless powder (71.4 %) 158-159 °C

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Table-5 (8)b

Example No.	IR ν cm ⁻¹	NMR (CDCl ₃) δ
116	(KBr) 2912, 2848, 1734, 1578, 1282, 1254, 1088, 1064, 1048, 1024, 738, 714	1.10-3.45(8H,m), 3.74(3H,s), 5.23-5.52 (1H,m), 6.47(1H,d,J=6Hz), 6.73, 6.91 (1Hx2,d,J=11Hz), 7.86(1H,d,J=6Hz), 7.11-8.18(9H,m),
117	(KBr) 3224, 3080, 3004, 2936, 1626, 1560, 1504, 1454, 1406, 1304, 1204, 1176, 1150, 1030, 966, 834, 804,	1.02-2.78(7H,m), 2.93-3.41(1H,m), 3.79 (3H,s), 5.05(1H,br), 6.56-7.75(4H,m), 8.24(1H,br)
118	(KBr) 3070, 2926, 1470, 1455, 1407, 1266, 1059, 1011, 747,	1.25-2.90(7H,m), 3.20-3.58(1H,m), 2.41 (3H,s), 3.71(3H,s), 3.96(4H,s), 5.48- 5.72(1H,d,J=10Hz), 7.62-8.07(4H,m), 8.38-8.68(1H,m), 9.00(1H,s)
119	(KBr) 2932, 1460, 1137, 1005, 119	1.20-2.69(7H,m), 2.21(3H,s), 2.90-3.21 (1H,m), 3.65(3H,s), 3.45-3.78(4H,s), 4.90-5.16(1H,m), 6.50-7.82(3H,m), 8.16 (1H,s)
120	(KBr) 3070, 2932, 1470, 1455, 1011, 996,	1.17-2.70(7H,m), 2.21(3H,s), 2.83-3.17 (1H,m), 3.47(3H,s), 4.90-5.17(1H,m), 6.48-7.76(3H,m), 8.17(1H,s)
121	(KBr) 3420, 1580, 1472, 1454, 1376, 1290, 1264, 1166, 1090, 1016, 972, 744,	1.00-3.60(6H,m), 4.40-4.96(3H,m), 6.70-7.08(3H,m), 7.33-7.65(2H,m), 8.26(1H,d,J=6Hz)
122	(KBr) 2962, 2926, 1434, 1410, 1380, 1266, 999, 798, 744,	0.80-1.05(3H,t,J=7Hz), 1.10-2.10(8H,m) 2.21-2.50(2H,t,J=8Hz), 2.44(3H,s), 2.53-2.93(1H,m), 3.40-3.71(1H,m), 4.98-5.18(1H,d,J=11Hz), 7.03-7.33(3H, m), 7.62-7.84(1H,m), 8.28(1H,s)

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Table-5 (9) a

Example No.	R	R ¹	R ²	R ³	A	Melting point (yield)
123	H	OCH ₂ CH ₂ OCH ₃	H	H	N	Brown amorphous powder (77.1 %) 97-99 °C
124	3-CH ₃	H	H	H	N	Yellow amorphous powder (42.4 %) 99-102 °C
125	3-CH ₃	OCH ₃	H	H	N	Palely yellow powder (78.8 %) 138-140 °C
126	3-CH ₃	OCH ₂ CF ₂ CF ₂ H	H	H	N	Colorless powder (83.7 %) 118-119 °C
127	H	OCH ₃	H	SO ₂ CH ₃	CH	Colorless powder (11.8 %) 159-161 °C

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EP 0 434 999 B1

Table-5 (9)b

Example No.	IR cm ⁻¹	NMR (CDCl ₃)
123	(KBr) 2920, 1580, 1452, 1270, 1123, 1059,	1.05-1.60(2H,m), 1.62-2.75(4H,m), 3.43(3H,s), 3.62-3.90(2H,m), 3.95-4.28(2H,m), 4.50-4.72(1H,d,J=10Hz), 6.56-6.80(1H,m), 7.07-7.30(1H,m), 7.80-8.52(3H,m)
124	(KBr) 2926, 1404, 1269, 1050, 957, 909, 888, 804, 74,	1.32-3.15(8H,m), 2.20(3H,s), 4.56-4.78(1H,d,J=9Hz), 7.23(3H,m), 7.80-8.26(2H,m), 8.40-8.60(6H,d,J=6Hz)
125	(KBr) 2943, 1600, 1477, 1440, 1410, 1268, 1059, 817,	1.30-2.75(7H,m), 1.69(3H,s), 2.21(3H,s), 3.06-3.21(1H,m), 4.60-4.80(1H,d, J=10Hz), 7.15-7.36(1H,t), 8.03-8.16(1H,d,J=7Hz), 8.16(1H,s), 8.43-8.60(1H,d,J=6Hz)
126	(KBr) 2935, 1590, 1454, 1407, 1269, 1195, 1107, 1051,	1.30-2.75(7H,m), 2.19(3H,s), 3.06-3.21(1H,m), 3.86-4.25(3H,t,J=12Hz), 5.30-6.70(2H,m), 7.13-7.40(1H,m), 8.00-8.28(2H,m), 8.45-8.60(1H,d,J=5Hz)
127	(KBr) 2988, 1584, 1476, 1434, 1358, 1286, 1250, 1234, 1170, 1046, 974, 812, 772, 538, 518	1.00-3.50(8H,m), 3.53(3H,s), 3.76(3H,s), 5.39(1H,d,J=10Hz), 6.51(1H,d,6Hz), 7.13-7.53(2H,m), 7.58-8.00(2H,m), 7.85(1H,d,J=6Hz)

In the table *1 CDCl₃ - acetone-d₆

*2 CDCl₃ - DMSO-d₆

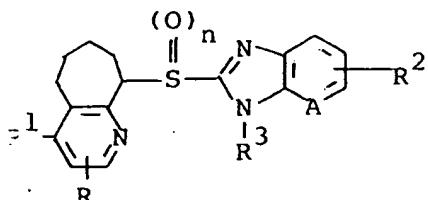
Claims

Claims for the following Contracting States : AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE

1. A cycloheptenopyridine derivative represented by the general formula

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[I]

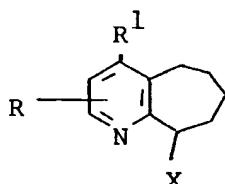
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[wherin R represents a hydrogen atom or lower alkyl group; R¹ represents a hydrogen atom, halogen atom, lower alkoxy group, lower cycloalkoxy group, amido group, substituted phenoxy group, substituted benzyloxy group, lower alkoxy group optionally containing halogen atom(s), nitro group, hydroxyl group, lower alkenyloxy group, lower alkylthio group, or group-NR⁴R⁵ (wherein R⁴ and R⁵ may be the same or different and each represents a hydrogen atom or lower alkyl group, or R⁴ and R⁵ mutually combine together with the nitrogen atom adjacent thereto to form a 5- or 6- membered cycle); R² represents a hydrogen atom, halogen atom, lower alkyl group optionally containing a halogen atom, lower alkoxy group optionally containing a halogen atom, hydroxyl group, acyl group, lower alkoxy carbonyl group, nitro group or amino group; R³ represents a lower alkyl group, lower alkoxy methyl group, lower alkylcarbonyl group, lower alkoxy carbonyl group, carbamoyl group, lower alkylcarbamoyl group, lower alkylcarbonylmethyl group, lower alkoxy carbonylmethyl group, lower acyloxymethyl group, lower alkylsulfonyl group, or physiologically acceptable protective group eliminable in an acid medium or under a physiological condition; n represents 0 or 1; and A represents a methine carbon or nitrogen atom] or a salt thereof.

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2. A process for preparation of a cycloheptenopyridine derivative of claim 1 or a salt thereof which comprises reacting a compound represented by the general formula

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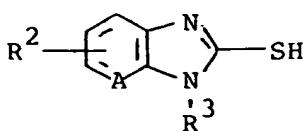


[II]

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[wherin R represents a hydrogen atom or lower alkyl group; R¹ represents a hydrogen atom, halogen atom, lower alkoxy group, lower cycloalkoxy group, amido group, substituted phenoxy group, substituted benzyloxy group, lower alkoxy group optionally containing halogen atom(s), nitro group, hydroxyl group, lower alkenyloxy group, lower alkylthio group, or group-NR⁴R⁵ (wherein R⁴ and R⁵ may be the same or different and each represents a hydrogen atom or lower alkyl group, or R⁴ and R⁵ mutually combine together with the nitrogen atom adjacent thereto to form a 5- or 6- membered cycle); and X represents a hydrogen atom, halogen atom, or alkylsulfonyl or arylsulfonyl group] with a compound represented by the formula

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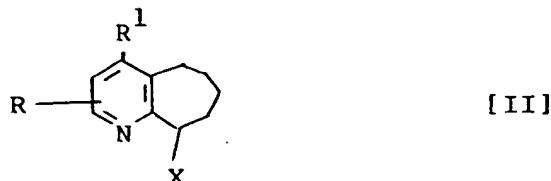
[III]

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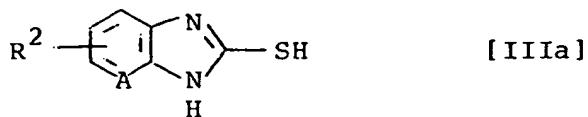
[wherein R² represents a hydrogen atom, halogen atom, lower alkyl group optionally containing a halogen atom, lower alkoxy group optionally containing a halogen atom, hydroxyl group, acyl group, lower alkoxy carbonyl group, nitro group or amino group; R³ represents a lower alkyl group, lower

alkoxymethyl group, lower alkylcarbonyl group, lower alkoxy carbonyl group, carbamoyl group, lower alkylcarbamoyl group, lower alkylcarbonylmethyl group, lower alkoxy carbonylmethyl group, lower acyloxymethyl group, lower alkylsulfonyl group, or physiologically acceptable protective group eliminable in an acid medium or under a physiological condition; and A represents methine carbon or a nitrogen atom], and then subjecting, if desired, the resulting compound to an oxidation reaction.

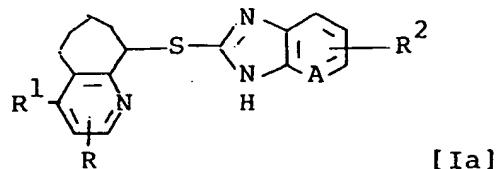
- 5 3. A process for preparation of a cycloheptenopyridine derivative of claim 1 or a salt thereof which comprises reacting a compound represented by the general formula



[wherein R represents a hydrogen atom or lower alkyl group; R¹ represents a hydrogen atom, halogen atom, lower alkoxy group, lower cycloalkoxy group, amido group, substituted phenoxy group, substituted benzyloxy group, lower alkoxy group optionally containing halogen atom(s), nitro group, hydroxyl group, lower alkenyloxy group, lower alkylthio group, or group-NR⁴R⁵ (wherein R⁴ and R⁵ may be the same or different and each represents a hydrogen atom or lower alkyl group, or R⁴ and R⁵ mutually combine together with the nitrogen atom adjacent thereto to form a 5- or 6-membered cycle); and X represents a hydrogen atom, halogen atom, or alkylsulfonyl or arylsulfonyl group] with a compound represented by the formula



[wherein R² represents a hydrogen atom, halogen atom, lower alkyl group optionally containing a halogen atom, lower alkoxy group optionally containing a halogen atom, hydroxyl group, acyl group, lower alkoxy carbonyl group, nitro group or amino group; and A represents methine carbon or a nitrogen atom], reacting the resulting cycloheptenopyridine derivative represented by the general formula



40 (wherein R, R¹, R² and A are as defined above) with a halide selected from lower alkyl halides, lower alkoxy methyl halides, lower alkylcarbonyl halides, lower alkoxy carbonyl halides, lower alkylcarbonylmethyl halides, lower alkoxy carbonylmethyl halides and lower alkylsulfonyl halides, and then, if desired, subjecting the resulting compound to an oxidation reaction.

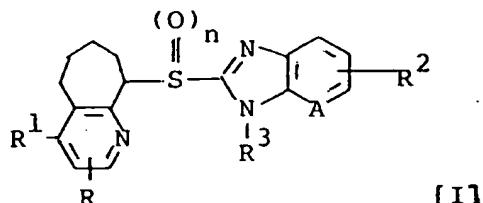
- 45 50 4. An antiulcer agent comprising a cycloheptenopyridine derivative of claim 1 or a salt thereof as an effective ingredient.

Claims for the following Contracting State : ES

1. A process for preparation of a cycloheptenopyridine derivative represented by the general formula

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[I]

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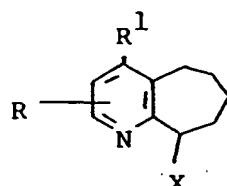
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[wherein R represents a hydrogen atom or lower alkyl group; R¹ represents a hydrogen atom, halogen atom, lower alkoxy group, lower cycloalkoxy group, amido group, substituted phenoxy group, substituted benzyloxy group, lower alkoxy group optionally containing halogen atom(s), nitro group, hydroxyl group, lower alkenyloxy group, lower alkylthio group, or group-NR⁴R⁵ (wherein R⁴ and R⁵ may be the same or different and each represents a hydrogen atom or lower alkyl group, or R⁴ and R⁵ mutually combine together with the nitrogen atom adjacent thereto to form a 5- or 6- membered cycle); R² represents a hydrogen atom, halogen atom, lower alkyl group optionally containing a halogen atom, lower alkoxy group optionally containing a halogen atom, hydroxyl group, acyl group, lower alkoxy carbonyl group, nitro group or amino group; R³ represents a lower alkyl group, lower alkoxy methyl group, lower alkylcarbonyl group, lower alkoxy carbonyl group, carbamoyl group, lower alkylcarbamoyl group, lower alkylcarbonylmethyl group, lower alkoxy carbonylmethyl group, lower acyloxymethyl group, lower alkylsulfonyl group, or physiologically acceptable protective group eliminable in an acid medium or under a physiological condition; n represents 0 or 1; and A represents a methine carbon or nitrogen atom] or a salt thereof, which comprises reacting a compound represented by the general formula



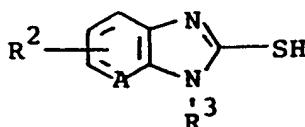
[II]

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[wherein R represents a hydrogen atom or lower alkyl group; R¹ represents a hydrogen atom, halogen atom, lower alkoxy group, lower cycloalkoxy group, amido group, substituted phenoxy group, substituted benzyloxy group, lower alkoxy group optionally containing halogen atom(s), nitro group, hydroxyl group, lower alkenyloxy group, lower alkylthio group, or group-NR⁴R⁵ (wherein R⁴ and R⁵ may be the same or different and each represents a hydrogen atom or lower alkyl group, or R⁴ and R⁵ mutually combine together with the nitrogen atom adjacent thereto to form a 5- or 6- membered cycle); and X represents a hydrogen atom, halogen atom, or alkylsulfonyl or arylsulfonyl group] with a compound represented by the formula

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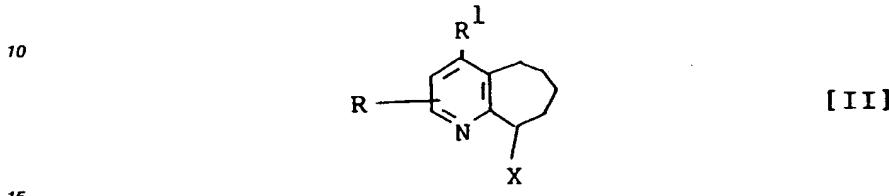
[III]

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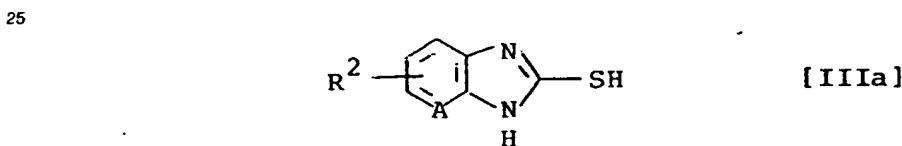
[wherein R² represents a hydrogen atom, halogen atom, lower alkyl group optionally containing a halogen atom, lower alkoxy group optionally containing a halogen atom, hydroxyl group, acyl group, lower alkoxy carbonyl group, nitro group or amino group; R³ represents a lower alkyl group, lower alkoxy methyl group, lower alkylcarbonyl group, lower alkoxy carbonyl group, carbamoyl group, lower alkylcarbamoyl group, lower alkylcarbonylmethyl group, lower alkoxy carbonylmethyl group, lower acyloxymethyl group, lower alkylsulfonyl group, or physiologically acceptable protective group eliminable in an acid medium or under a physiological condition]

acyloxyethyl group, lower alkylsulfonyl group, or physiologically acceptable protective group eliminable in an acid medium or under a physiological condition; and A represents methine carbon or a nitrogen atom], and then subjecting, if desired, the resulting compound to an oxidation reaction.

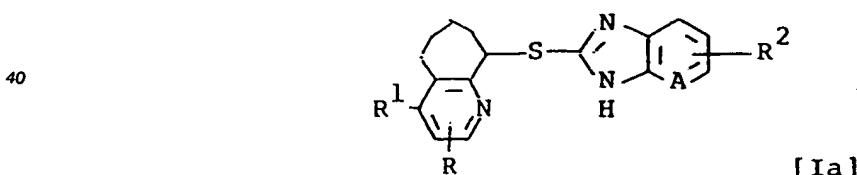
- 5 2. A process for preparation of a cycloheptenopyridine derivative of claim 1 or a salt thereof which comprises reacting a compound represented by the general formula



[wherein R represents a hydrogen atom or lower alkyl group; R¹ represents a hydrogen atom, halogen atom, lower alkoxy group, lower cycloalkoxy group, amido group, substituted phenoxy group, substituted benzyloxy group, lower alkoxy group optionally containing halogen atom(s), nitro group, hydroxyl group, lower alkenyloxy group, lower alkylthio group, or group-NR⁴R⁵ (wherein R⁴ and R⁵ may be the same or different and each represents a hydrogen atom or lower alkyl group, or R⁴ and R⁵ mutually combine together with the nitrogen atom adjacent thereto to form a 5- or 6- membered cycle); and X represents a hydrogen atom, halogen atom, or alkylsulfonyl or arylsulfonyl group] with a compound represented by the formula



[wherein R² represents a hydrogen atom, halogen atom, lower alkyl group optionally containing a halogen atom, lower alkoxy group optionally containing a halogen atom, hydroxyl group, acyl group, lower alkoxy carbonyl group, nitro group or amino group; and A represents methine carbon or a nitrogen atom], reacting the resulting cycloheptenopyridine derivative represented by the general formula



(wherein R, R¹, R² and A are as defined above) with a halide selected from lower alkyl halides, lower alkoxy methyl halides, lower alkyl carbonyl halides, lower alkoxy carbonyl halides, lower alkyl carbonyl-methyl halides, lower alkoxy carbonyl methyl halides and lower alkylsulfonyl halides, and then, if desired, subjecting the resulting compound to an oxidation reaction.

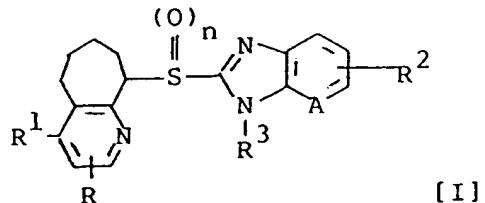
- 50 3. A process for preparing an antiulcer agent comprising mixing a cycloheptenopyridine derivative prepared according to claim 1 or a salt thereof as an effective ingredient and a carrier and/or diluent.

Claims for the following Contracting State : GR

1. A cycloheptenopyridine derivative represented by the general formula

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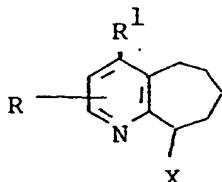


[I]

15 [wherein R represents a hydrogen atom or lower alkyl group; R¹ represents a hydrogen atom, halogen atom, lower alkoxy group, lower cycloalkoxy group, amido group, substituted phenoxy group, substituted benzyloxy group, lower alkoxy group optionally containing halogen atom(s), nitro group, hydroxyl group, lower alkenyloxy group, lower alkylthio group, or group-NR⁴R⁵ (wherein R⁴ and R⁵ may be the same or different and each represents a hydrogen atom or lower alkyl group, or R⁴ and R⁵ mutually combine together with the nitrogen atom adjacent thereto to form a 5- or 6- membered cycle); R² represents a hydrogen atom, halogen atom, lower alkyl group optionally containing a halogen atom, lower alkoxy group optionally containing a halogen atom, hydroxyl group, acyl group, lower alkoxy carbonyl group, nitro group or amino group; R³ represents a lower alkyl group, lower alkoxy methyl group, lower alkyl carbonyl group, lower alkoxy carbonyl group, carbamoyl group, lower alkyl carbamoyl group, lower alkyl carbonylmethyl group, lower alkoxy carbonylmethyl group, lower acyloxymethyl group, lower alkylsulfonyl group, or physiologically acceptable protective group eliminable in an acid medium or under a physiological condition; n represents 0 or 1; and A represents a methine carbon or nitrogen atom] or a salt thereof.

20 2. A process for preparation of a cycloheptenopyridine derivative of claim 1 or a salt thereof which comprises reacting a compound represented by the general formula

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[II]

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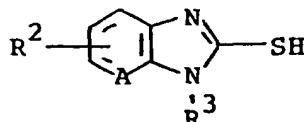
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[wherein R represents a hydrogen atom or lower alkyl group; R¹ represents a hydrogen atom, halogen atom, lower alkoxy group, lower cycloalkoxy group, amido group, substituted phenoxy group, substituted benzyloxy group, lower alkoxy group optionally containing halogen atom(s), nitro group, hydroxyl group, lower alkenyloxy group, lower alkylthio group, or group-NR⁴R⁵ (wherein R⁴ and R⁵ may be the same or different and each represents a hydrogen atom or lower alkyl group, or R⁴ and R⁵ mutually combine together with the nitrogen atom adjacent thereto to form a 5- or 6- membered cycle); and X represents a hydrogen atom, halogen atom, or alkylsulfonyl or arylsulfonyl group] with a compound represented by the formula

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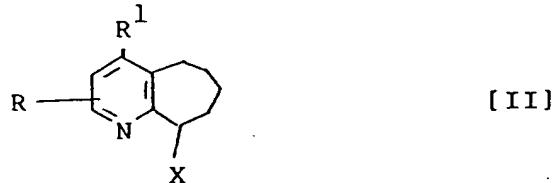
[III]

[wherein R² represents a hydrogen atom, halogen atom, lower alkyl group optionally containing a halogen atom, lower alkoxy group optionally containing a halogen atom, hydroxyl group, acyl group,

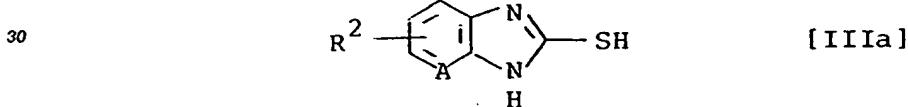
lower alkoxy carbonyl group, nitro group or amino group; R³ represents a lower alkyl group, lower alkoxy methyl group, lower alkyl carbonyl group, lower alkoxy carbonyl group, carbamoyl group, lower alkyl carbamoyl group, lower alkyl carbonylmethyl group, lower alkoxy carbonylmethyl group, lower acyloxymethyl group, lower alkylsulfonyl group, or physiologically acceptable protective group eliminable in an acid medium or under a physiological condition; and A represents methine carbon or a nitrogen atom], and then subjecting, if desired, the resulting compound to an oxidation reaction.

3. A process for preparation of a cycloheptenopyridine derivative of claim 1 or a salt thereof which comprises reacting a compound represented by the general formula

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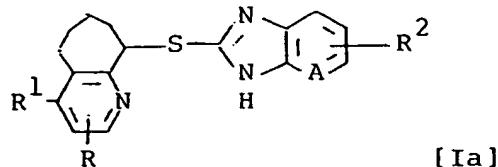


20 [wherein R represents a hydrogen atom or lower alkyl group; R¹ represents a hydrogen atom, halogen atom, lower alkoxy group, lower cycloalkoxy group, amido group, substituted phenoxy group, substituted benzyloxy group, lower alkoxy group optionally containing halogen atom(s), nitro group, hydroxyl group, lower alkenyloxy group, lower alkylthio group, or group-NR⁴R⁵ (wherein R⁴ and R⁵ may be the same or different and each represents a hydrogen atom or lower alkyl group, or R⁴ and R⁵ mutually combine together with the nitrogen atom adjacent thereto to form a 5- or 6-membered cycle); and X represents a hydrogen atom, halogen atom, or alkylsulfonyl or arylsulfonyl group] with a compound represented by the formula



35 [wherein R² represents a hydrogen atom, halogen atom, lower alkyl group optionally containing a halogen atom, lower alkoxy group optionally containing a halogen atom, hydroxyl group, acyl group, lower alkoxy carbonyl group, nitro group or amino group; and A represents methine carbon or a nitrogen atom], reacting the resulting cycloheptenopyridine derivative represented by the general formula

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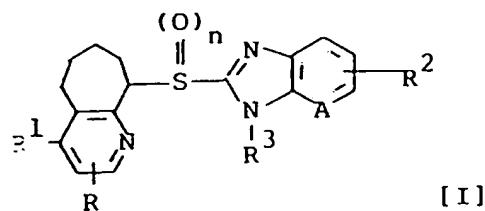
50 (wherein R, R¹, R² and A are as defined above) with a halide selected from lower alkyl halides, lower alkoxy methyl halides, lower alkyl carbonyl halides, lower alkoxy carbonyl halides, lower alkyl carbonyl methyl halides, lower alkoxy carbonyl methyl halides and lower alkylsulfonyl halides, and then, if desired, subjecting the resulting compound to an oxidation reaction.

- 55 4. An agent comprising a cycloheptenopyridine derivative of claim 1 or a salt thereof as an effective ingredient.

Patentansprüche**Patentansprüche für folgende Vertragsstaaten : AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE**

1. Cyloheptenopyridinderivat, das durch die allgemeine Formel:

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dargestellt wird [worin R ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeutet; R' ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkoxygruppe, eine Niedrigcycloalkoxygruppe, eine Amido-gruppe, eine substituierte Phenoxygruppe, eine substituierte Benzyloxygruppe, eine Niedrigalkoxygruppe, die gegebenenfalls ein oder mehrere Halogenatom(e) enthalten kann, eine Nitrogruppe, eine Hydroxylgruppe, eine Niedrigalkenyloxygruppe, eine Niedrigalkylthiogruppe oder eine Gruppe -NR⁴R⁵ - (worin R⁴ und R⁵ gleich oder unterschiedlich sein können und je ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeuten oder worin R⁴ und R⁵ gemeinsam mit dem benachbarten Stickstoffatom einen 5- oder 6gliedrigen Ring bilden) bedeutet; R² ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkylgruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Niedrigalkoxygruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Hydroxylgruppe, eine Acylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Nitrogruppe oder eine Aminogruppe bedeutet; R³ eine Niedrigalkylgruppe, eine Niedrigalkoxymethylgruppe, eine Niedrigalkylcarbonylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Carbamoylgruppe, eine Niedrigalkylcarbamoylgruppe, eine Niedrigalkylcarbonylmethylgruppe, eine Niedrigalkoxycarbonylmethylgruppe, eine Niedrigacyloxymethylgruppe, eine Niedrigalkylsulfonylgruppe oder eine physiologisch annehmbare Schutzgruppe, die in saurem Medium oder unter physiologischen Bedingungen abspaltbar ist, bedeutet; n 0 oder 1 bedeutet; und A ein Methin-Kohlenstoffatom oder ein Stickstoffatom bedeutet], oder ein Salz davon.

2. Verfahren zur Herstellung eines Cycloheptenopyridinderivats nach Anspruch 1 oder eines Salzes davon, dadurch gekennzeichnet, daß eine Verbindung, die durch die allgemeine Formel:

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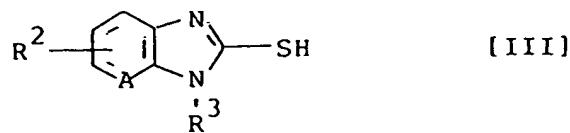


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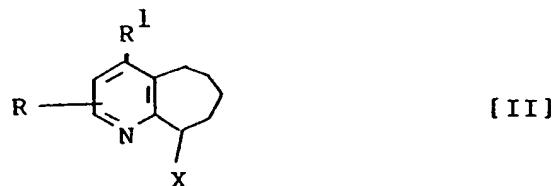
dargestellt wird [worin R ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeutet; R' ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkoxygruppe, eine Niedrigcycloalkoxygruppe, eine Amido-gruppe, eine substituierte Phenoxygruppe, eine substituierte Benzyloxygruppe, eine Niedrigalkoxygruppe, die gegebenenfalls ein oder mehrere Halogenatom(e) enthalten kann, eine Nitrogruppe, eine Hydroxylgruppe, eine Niedrigalkenyloxygruppe, eine Niedrigalkylthiogruppe oder eine Gruppe -NR⁴R⁵ - (worin R⁴ und R⁵ gleich oder unterschiedlich sein können und je ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeuten oder worin R⁴ und R⁵ gemeinsam mit dem benachbarten Stickstoffatom einen 5- oder 6gliedrigen Ring bilden) bedeutet; und X ein Wasserstoffatom, ein Halogenatom oder eine Alkylsulfonyl- oder Arylsulfonylgruppe bedeutet], mit einer Verbindung, die durch die Formel:

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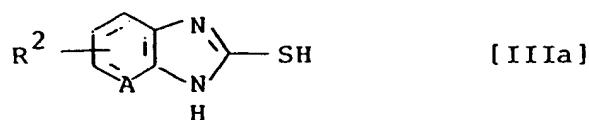


dargestellt wird [worin R^2 ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkylgruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Niedrigalkoxygruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Hydroxylgruppe, eine Acylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Nitrogruppe oder eine Aminogruppe bedeutet; R^3 eine Niedrigalkylgruppe, eine Niedrigalkoxymethylgruppe, eine Niedrigalkylcarbamoylgruppe, eine Niedrigalkylcarbonylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Carbamoylgruppe, eine Niedrigalkylcarbamoylgruppe, eine Niedrigalkylcarbonylmethylgruppe, eine Niedrigalkoxycarbonylmethylgruppe, eine Niedrigacyloxymethylgruppe, eine Niedrigalkylsulfonylgruppe oder eine physiologisch annehmbare Schutzgruppe, die in saurem Medium oder unter physiologischen Bedingungen abspaltbar ist, bedeutet; und A ein Methin-Kohlenstoffatom oder ein Stickstoffatom bedeutet], umgesetzt wird und dann gewünschtenfalls die entstehende Verbindung einer Oxidationsreaktion unterworfen wird.

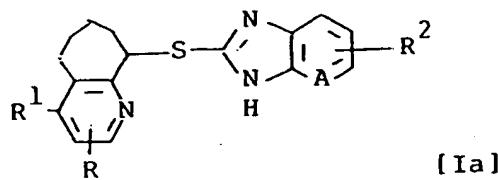
- 10 3. Verfahren zur Herstellung eines Cycloheptenopyridinderivats nach Anspruch 1 oder eines Salzes davon, dadurch gekennzeichnet, daß eine Verbindung, die durch die allgemeine Formel:



- 30 dargestellt wird [worin R ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeutet; R^1 ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkoxygruppe, eine Niedrigcycloalkoxygruppe, eine Amido-gruppe, eine substituierte Phenoxygruppe, eine substituierte Benzyoxygruppe, eine Niedrigalkoxygruppe, die gegebenenfalls ein oder mehrere Halogenatom(e) enthalten kann, eine Nitrogruppe, eine Hydroxylgruppe, eine Niedrigalkyloxygruppe, eine Niedrigalkylthiogruppe oder eine Gruppe $-NR^4R^5-$ (worin R^4 und R^5 gleich oder unterschiedlich sein können und je ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeuten oder worin R^4 und R^5 gemeinsam mit dem benachbarten Stickstoffatom einen 5- oder 6gliedrigen Ring bilden) bedeutet; und X ein Wasserstoffatom, ein Halogenatom oder eine Alkylsulfonyl- oder Arylsulfonylgruppe bedeutet], mit einer Verbindung, die durch die Formel:



- 45 dargestellt wird [worin R^2 ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkylgruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Niedrigalkoxygruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Hydroxylgruppe, eine Acylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Nitrogruppe oder eine Aminogruppe bedeutet; und A ein Methin-Kohlenstoffatom oder ein Stickstoff-atom bedeutet], umgesetzt wird und das entstehende Cycloheptenopyridinderivat, das durch die allgemeine Formel:

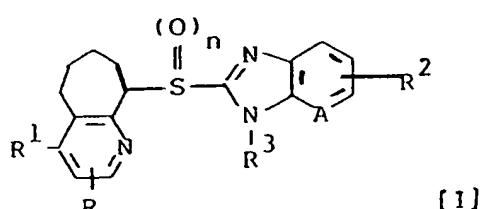


10 dargestellt wird (worin R, R¹, R² und A die oben gegebenen Definitionen besitzen), mit einem Halogenid, ausgewählt aus Niedrigalkylhalogeniden, Niedrigalkoxymethylhalogeniden, Niedrigalkylcarbonylhalogeniden, Niedrigalkoxycarbonylhalogeniden, Niedrigalkylcarbonylmethylhalogeniden, Niedrigalkoxycarbonylmethylhalogeniden und Niedrigalkylsulfonylhalogeniden, umgesetzt wird und dann gewünschtenfalls die entstehende Verbindung einer Oxidationsreaktion unterworfen wird.

- 15 4. Anti-Ulkusmittel, dadurch gekennzeichnet, daß es ein Cycloheptenopyridinderivat nach Anspruch 1 oder ein Salz davon als wirksamen Bestandteil enthält.

Patentansprüche für folgenden Vertragsstaat : ES

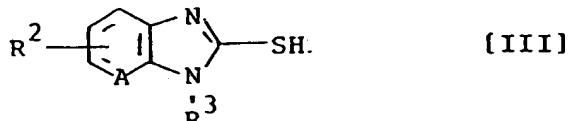
- 20 1. Verfahren zur Herstellung eines Cycloheptenopyridinderivats, das durch die allgemeine Formel:



30 dargestellt wird [worin R ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeutet; R¹ ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkoxygruppe, eine Niedrigcycloalkoxygruppe, eine Amido-gruppe, eine substituierte Phenoxygruppe, eine substituierte Benzyloxygruppe, eine Niedrigalkoxygruppe, die gegebenenfalls ein oder mehrere Halogenatom(e) enthalten kann, eine Nitrogruppe, eine Hydroxylgruppe, eine Niedrigalkenyloxygruppe, eine Niedrigalkylthiogruppe oder eine Gruppe -NR⁴R⁵ - (worin R⁴ und R⁵ gleich oder unterschiedlich sein können und je ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeuten oder worin R⁴ und R⁵ gemeinsam mit dem benachbarten Stickstoffatom einen 5- oder 6gliedrigen Ring bilden); R² ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkylgruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Niedrigalkoxygruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Hydroxylgruppe, eine Acylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Nitrogruppe oder eine Aminogruppe bedeutet; R³ eine Niedrigalkylgruppe, eine Niedrigalkoxymethylgruppe, eine Niedrigalkylcarbonylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Carbamoylgruppe, eine Niedrigalkylcarbamoylgruppe, eine Niedrigalkylcarbonylmethylgruppe, eine Niedrigalkoxycarbonylmethylgruppe, eine Niedrigacyloxymethylgruppe, eine Niedrigalkylsulfonylgruppe oder eine physiologisch annehmbare Schutzgruppe, die in saurem Medium oder unter physiologischen Bedingungen abspaltbar ist, bedeutet; n 0 oder 1 bedeutet; und A ein Methin-Kohlenstoffatom oder ein Stickstoffatom bedeutet], oder eines Salzes davon, dadurch gekennzeichnet, daß eine Verbindung, die durch die allgemeine Formel:

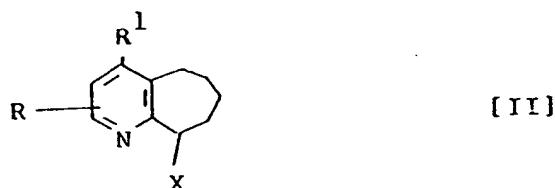


dargestellt wird [worin R ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeutet; R¹ ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkoxygruppe, eine Niedrigcycloalkoxygruppe, eine Amido-gruppe, eine substituierte Phenoxygruppe, eine substituierte Benzyloxygruppe, eine Niedrigalkoxygruppe, die gegebenenfalls ein oder mehrere Halogenatom(e) enthalten kann, eine Nitrogruppe, eine Hydroxylgruppe, eine Niedrigalkenyloxygruppe, eine Niedrigalkylthiogruppe oder eine Gruppe -NR⁴R⁵ - (worin R⁴ und R⁵ gleich oder unterschiedlich sein können und je ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeuten oder worin R⁴ und R⁵ gemeinsam mit dem benachbarten Stickstoffatom einen 5- oder 6gliedrigen Ring bilden) bedeutet; und X ein Wasserstoffatom, ein Halogenatom oder eine Alkylsulfonyl- oder Arylsulfonylgruppe bedeutet], mit einer Verbindung, die durch die Formel:

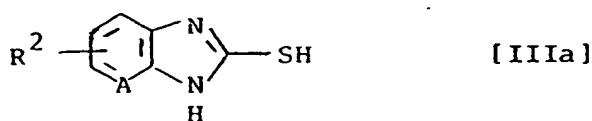


dargestellt wird [worin R² ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkylgruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Niedrigalkoxygruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Hydroxylgruppe, eine Acylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Nitrogruppe oder eine Aminogruppe bedeutet; R³ eine Niedrigalkylgruppe, eine Niedrigalkoxymethylgruppe, eine Niedrigalkylcarbonylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Carbamoylgruppe, eine Niedrigalkylcarbamoylgruppe, eine Niedrigalkylcarbonylmethylgruppe, eine Niedrigalkoxycarbonylmethylgruppe, eine Niedrigacyloxymethylgruppe, eine Niedrigalkylsulfonylgruppe oder eine physiologisch annehmbare Schutzgruppe, die in saurem Medium oder unter physiologischen Bedingungen abspaltbar ist, bedeutet; und A ein Methin-Kohlenstoffatom oder ein Stickstoffatom bedeutet], umgesetzt wird und dann gewünschtenfalls die entstehende Verbindung einer Oxidationsreaktion unterworfen wird.

2. Verfahren zur Herstellung eines Cycloheptenopyridinderivats nach Anspruch 1 oder eines Salzes davon, dadurch gekennzeichnet, daß eine Verbindung, die durch die allgemeine Formel:



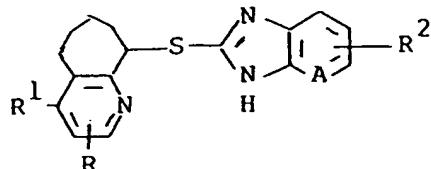
dargestellt wird [worin R ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeutet; R¹ ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkoxygruppe, eine Niedrigcycloalkoxygruppe, eine Amido-gruppe, eine substituierte Phenoxygruppe, eine substituierte Benzyloxygruppe, eine Niedrigalkoxygruppe, die gegebenenfalls ein oder mehrere Halogenatom(e) enthalten kann, eine Nitrogruppe, eine Hydroxylgruppe, eine Niedrigalkenyloxygruppe, eine Niedrigalkylthiogruppe oder eine Gruppe -NR⁴R⁵ - (worin R⁴ und R⁵ gleich oder unterschiedlich sein können und je ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeuten oder worin R⁴ und R⁵ gemeinsam mit dem benachbarten Stickstoffatom einen 5- oder 6gliedrigen Ring bilden) bedeutet; und X ein Wasserstoffatom, ein Halogenatom oder eine Alkylsulfonyl- oder Arylsulfonylgruppe bedeutet], mit einer Verbindung, die durch die Formel:



dargestellt wird [worin R² ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkylgruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Niedrigalkoxygruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Hydroxylgruppe, eine Acylgruppe, eine Niedrigalkoxycarbonylgruppe, eine

Nitrogruppe oder eine Aminogruppe bedeutet; und A ein Methin-Kohlenstoffatom oder ein Stickstoffatom bedeutet], umgesetzt wird und das entstehende Cycloheptenopyridinderivat, das durch die allgemeine Formel:

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{ Ia }

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dargestellt wird (worin R, R¹, R² und A die oben gegebenen Definitionen besitzen), mit einem Halogenid, ausgewählt aus Niedrigalkylhalogeniden, Niedrigalkoxymethylhalogeniden, Niedrigalkylcarbonylhalogeniden, Niedrigalkoxycarbonylhalogeniden, Niedrigalkylcarbonylmethylhalogeniden, Niedrigalkoxycarbonylmethylhalogeniden und Niedrigalkylsulfonylhalogeniden, umgesetzt wird und dann gewünschtenfalls die entstehende Verbindung einer Oxidationsreaktion unterworfen wird.

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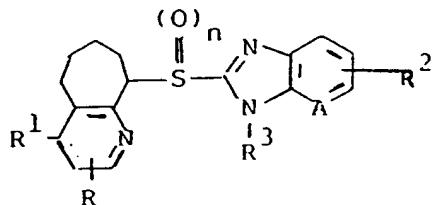
3. Verfahren zur Herstellung eines Anti-Ulkusmittels, dadurch gekennzeichnet, daß ein Cycloheptenopyridinderivat, hergestellt nach Anspruch 1, oder ein Salz davon als wirksamer Bestandteil und ein Träger und/oder ein Verdünnungsmittel vermischt werden.

Patentansprüche für folgenden Vertragsstaat : GR

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1. Cycloheptenopyridinderivat, das durch die allgemeine Formel:

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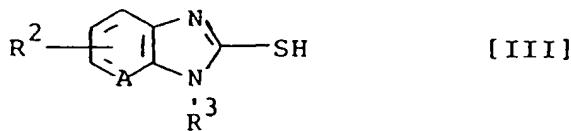
dargestellt wird [worin R ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeutet; R¹ ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkoxygruppe, eine Niedrigcycloalkoxygruppe, eine Amido-gruppe, eine substituierte Phenoxygruppe, eine substituierte Benzyloxygruppe, eine Niedrigalkoxygruppe, die gegebenenfalls ein oder mehrere Halogenatom(e) enthalten kann, eine Nitrogruppe, eine Hydroxylgruppe, eine Niedrigalkenyloxygruppe, eine Niedrigalkylthiogruppe oder eine Gruppe -NR⁴R⁵ - (worin R⁴ und R⁵ gleich oder unterschiedlich sein können und je ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeuten oder worin R⁴ und R⁵ gemeinsam mit dem benachbarten Stickstoffatom einen 5- oder 6gliedrigen Ring bilden) bedeutet; R² ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkylgruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Niedrigalkoxygruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Hydroxylgruppe, eine Acylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Nitrogruppe oder eine Aminogruppe bedeutet; R³ eine Niedrigalkylgruppe, eine Niedrigalkoxymethylgruppe, eine Niedrigalkylcarbonylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Carbamoylgruppe, eine Niedrigalkylcarbamoylgruppe, eine Niedrigalkylcarbonylmethylgruppe, eine Niedrigalkoxycarbonylmethylgruppe, eine Niedrigacyloxymethylgruppe, eine Niedrigalkylsulfonylgruppe oder eine physiologisch annehmbare Schutzgruppe, die in saurem Medium oder unter physiologischen Bedingungen abspaltbar ist, bedeutet; n 0 oder 1 bedeutet; und A ein Methin-Kohlenstoffatom oder ein Stickstoffatom bedeutet], oder ein Salz davon.

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2. Verfahren zur Herstellung eines Cycloheptenopyridinderivats nach Anspruch 1 oder eines Salzes davon, dadurch gekennzeichnet, daß eine Verbindung, die durch die allgemeine Formel:

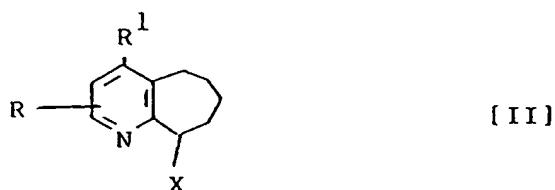


10 dargestellt wird [worin R ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeutet; R¹ ein Wasser-
stoffatom, ein Halogenatom, eine Niedrigalkoxygruppe, eine Niedrigcycloalkoxygruppe, eine Amido-
gruppe, eine substituierte Phenoxygruppe, eine substituierte Benzyloxygruppe, eine Niedrigalkoxygrup-
pe, die gegebenenfalls ein oder mehrere Halogenatom(e) enthalten kann, eine Nitrogruppe, eine
15 Hydroxylgruppe, eine Niedrigalkenyloxygruppe, eine Niedrigalkylthiogruppe oder eine Gruppe -NR⁴R⁵ -
(worin R⁴ und R⁵ gleich oder unterschiedlich sein können und je ein Wasserstoffatom oder eine
Niedrigalkylgruppe bedeuten oder worin R⁴ und R⁵ gemeinsam mit dem benachbarten Stickstoffatom
einen 5- oder 6gliedrigen Ring bilden) bedeutet; und X ein Wasserstoffatom, ein Halogenatom oder
eine Alkylsulfonyl- oder Arylsulfonylgruppe bedeutet], mit einer Verbindung, die durch die Formel:



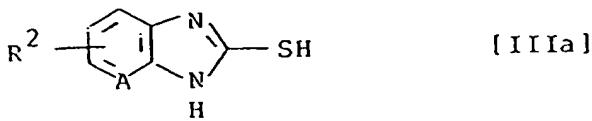
25 dargestellt wird [worin R² ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkylgruppe, die gegebe-
nenfalls ein Halogenatom enthalten kann, eine Niedrigalkoxygruppe, die gegebenenfalls ein Halogen-
atom enthalten kann, eine Hydroxylgruppe, eine Acylgruppe, eine Niedrigalkoxycarbonylgruppe, eine
Nitrogruppe oder eine Aminogruppe bedeutet; R³ eine Niedrigalkylgruppe, eine Niedrigalkoxymethyl-
30 gruppe, eine Niedrigalkylcarbonylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Carbamoylgruppe,
eine Niedrigalkylcarbamoylgruppe, eine Niedrigalkylcarbonylmethylgruppe, eine Niedrigalkoxycarbonyl-
methylgruppe, eine Niedrigacyloxymethylgruppe, eine Niedrigalkylsulfonylgruppe oder eine physiolo-
gisch annehmbare Schutzgruppe, die in saurem Medium oder unter physiologischen Bedingungen
35 abspaltbar ist, bedeutet; und A ein Methin-Kohlenstoffatom oder ein Stickstoffatom bedeutet], umge-
setzt wird und dann gewünschtenfalls die entstehende Verbindung einer Oxidationsreaktion unterworfen
wird.

3. Verfahren zur Herstellung eines Cycloheptenopyridinderivats nach Anspruch 1 oder eines Salzes
davon, dadurch gekennzeichnet, daß eine Verbindung, die durch die allgemeine Formel:



45 dargestellt wird [worin R ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeutet; R¹ ein Wasser-
stoffatom, ein Halogenatom, eine Niedrigalkoxygruppe, eine Niedrigcycloalkoxygruppe, eine Amido-
gruppe, eine substituierte Phenoxygruppe, eine substituierte Benzyloxygruppe, eine Niedrigalkoxygrup-
pe, die gegebenenfalls ein oder mehrere Halogenatom(e) enthalten kann, eine Nitrogruppe, eine
50 Hydroxylgruppe, eine Niedrigalkenyloxygruppe, eine Niedrigalkylthiogruppe oder eine Gruppe -NR⁴R⁵ -
(worin R⁴ und R⁵ gleich oder unterschiedlich sein können und je ein Wasserstoffatom oder eine
Niedrigalkylgruppe bedeuten oder worin R⁴ und R⁵ gemeinsam mit dem benachbarten Stickstoffatom
einen 5- oder 6gliedrigen Ring bilden) bedeutet; und X ein Wasserstoffatom, ein Halogenatom oder
eine Alkylsulfonyl- oder Arylsulfonylgruppe bedeutet], mit einer Verbindung, die durch die Formel:

5

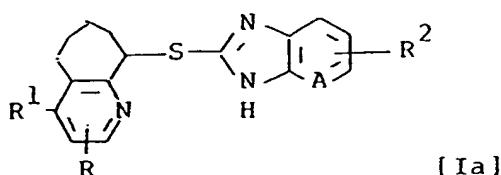


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dargestellt wird [worin R² ein Wasserstoffatom, ein Halogenatom, eine Niedrigalkylgruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Niedrigalkoxygruppe, die gegebenenfalls ein Halogenatom enthalten kann, eine Hydroxylgruppe, eine Acylgruppe, eine Niedrigalkoxycarbonylgruppe, eine Nitrogruppe oder eine Aminogruppe bedeutet; und A ein Methin-Kohlenstoffatom oder ein Stickstoffatom bedeutet], umgesetzt wird und das entstehende Cycloheptenopyridinderivat, das durch die allgemeine Formel:

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dargestellt wird (worin R, R¹, R² und A die oben gegebenen Definitionen besitzen), mit einem Halogenid, ausgewählt aus Niedrigalkylhalogeniden, Niedrigalkoxymethylhalogeniden, Niedrigalkylcarbonylhalogeniden, Niedrigalkoxycarbonylhalogeniden, Niedrigalkylcarbonylmethylhalogeniden, Niedrigalkoxycarbonylmethylhalogeniden und Niedrigalkylsulfonylhalogeniden, umgesetzt wird und dann gewünschtenfalls die entstehende Verbindung einer Oxidationsreaktion unterworfen wird.

30

4. Mittel, dadurch gekennzeichnet, daß es ein Cycloheptenopyridinderivat nach Anspruch 1 oder ein Salz davon als wirksamen Bestandteil enthält.

Revendications

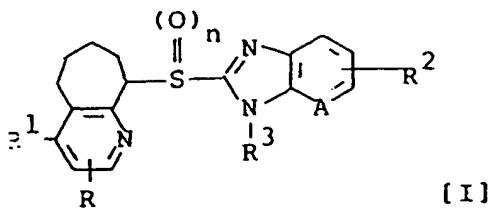
Revendications pour les Etats contractants suivants : AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE

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1. Dérivé de cyclohepténopyridine représenté par la formule générale :

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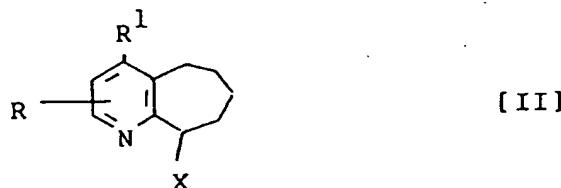
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[dans laquelle R représente un atome d'hydrogène ou un groupe alkyle inférieur ; R¹ représente un atome d'hydrogène, un atome d'halogène, un groupe alkoxy inférieur, un groupe cycloalcoxy inférieur, un groupe amido, un groupe phénoxy substitué, un groupe benzyloxy substitué, un groupe alkoxy inférieur contenant facultativement un ou plusieurs atomes d'halogène, un groupe nitro, un groupe hydroxyle, un groupe alcényloxy inférieur, un groupe alkylthio inférieur ou un groupe -NR⁴R⁵ (où R⁴ et R⁵ peuvent être identiques ou différents et représentent chacun un atome d'hydrogène ou un groupe alkyle inférieur, ou bien R⁴ et R⁵ sont pris ensemble avec l'atome d'azote qui leur est adjacent pour former un cycle penta- ou hexagonal) ; R² représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle inférieur contenant facultativement un atome d'halogène, un groupe alkoxy inférieur contenant facultativement un atome d'halogène, un groupe hydroxyle, un groupe acyle, un groupe alcoxycarbonyle inférieur, un groupe nitro ou un groupe amino ; R³ représente un groupe alkyle

inférieur, un groupe alcoxyméthyle inférieur, un groupe alkylcarbonyl inférieur, un groupe alcoxycarbonyl inférieur, un groupe carbamoyle, un groupe alkylcarbamoyl inférieur, un groupe alkylcarbonylméthyle inférieur, un groupe alcoxycarbonylméthyle inférieur, un groupe acyloxyméthyle inférieur, un groupe alkylsulfonyl inférieur, ou un groupe protecteur physiologiquement acceptable pouvant être éliminé en milieu acide ou dans des conditions physiologiques ; n représente 0 ou 1 ; et A représente un atome de carbone de méthine ou un atome d'azote] ou un sel de celui-ci.

- 5 2. Procédé de préparation d'un dérivé de cyclohepténopyridine de la revendication 1 ou d'un sel de celui-ci, qui consiste à faire réagir un composé représenté par la formule générale :

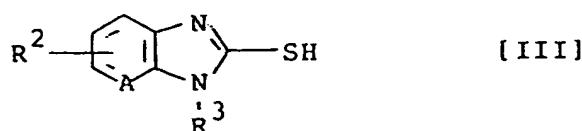
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[dans laquelle R représente un atome d'hydrogène ou un groupe alkyle inférieur ; R¹ représente un atome d'hydrogène, un atome d'halogène, un groupe alcoxy inférieur, un groupe cycloalcoxy inférieur, un groupe amido, un groupe phénoxy substitué, un groupe benzyloxy substitué, un groupe alcoxy inférieur contenant facultativement un ou plusieurs atomes d'halogène, un groupe nitro, un groupe hydroxyle, un groupe alcényloxy inférieur, un groupe alkylthio inférieur ou un groupe -NR⁴R⁵ (où R⁴ et R⁵ peuvent être identiques ou différents et représentent chacun un atome d'hydrogène ou un groupe alkyle inférieur, ou bien R⁴ et R⁵ sont pris ensemble avec l'atome d'azote qui leur est adjacent pour former un cycle penta- ou hexagonal) ; et X représente un atome d'hydrogène, un atome d'halogène ou un groupe alkylsulfonyl ou arylsulfonyl] avec un composé représenté par la formule :

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[dans laquelle R² représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle inférieur contenant facultativement un atome d'halogène, un groupe alcoxy inférieur contenant facultativement un atome d'halogène, un groupe hydroxyle, un groupe acyle, un groupe alcoxycarbonyl inférieur, un groupe nitro ou un groupe amino ; R³ représente un groupe alkyle inférieur, un groupe alcoxyméthyle inférieur, un groupe alkylcarbonyl inférieur, un groupe alcoxycarbonyl inférieur, un groupe carbamoyle, un groupe alkylcarbamoyl inférieur, un groupe alkylcarbonylméthyle inférieur, un groupe alcoxycarbonylméthyle inférieur, un groupe acyloxyméthyle inférieur, un groupe alkylsulfonyl inférieur, ou un groupe protecteur physiologiquement acceptable pouvant être éliminé en milieu acide ou dans des conditions physiologiques ; et A représente un atome de carbone de méthine ou un atome d'azote], puis à soumettre facultativement le composé résultant à une réaction d'oxydation.

40

- 45 3. Procédé de préparation d'un dérivé de cyclohepténopyridine de la revendication 1 ou d'un sel de celui-ci, qui consiste à faire réagir un composé représenté par la formule générale :

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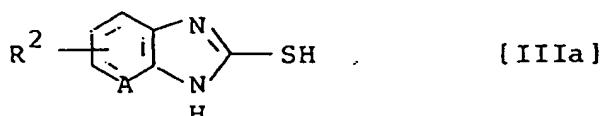


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[dans laquelle R représente un atome d'hydrogène ou un groupe alkyle inférieur ; R¹ représente un

atome d'hydrogène, un atome d'halogène, un groupe alcoxy inférieur, un groupe cycloalcoxy inférieur, un groupe amido, un groupe phénoxy substitué, un groupe benzyloxy substitué, un groupe alcoxy inférieur contenant facultativement un ou plusieurs atomes d'halogène, un groupe nitro, un groupe hydroxyle, un groupe alcényloxy inférieur, un groupe alkylthio inférieur ou un groupe -NR⁴R⁵ (où R⁴ et R⁵ peuvent être identiques ou différents et représentent chacun un atome d'hydrogène ou un groupe alkyle inférieur, ou bien R⁴ et R⁵ sont pris ensemble avec l'atome d'azote qui leur est adjacent pour former un cycle penta- ou hexagonal) ; et X représente un atome d'hydrogène, un atome d'halogène ou un groupe alkylsulfonyle ou arylsulfonyle] avec un composé représenté par la formule :

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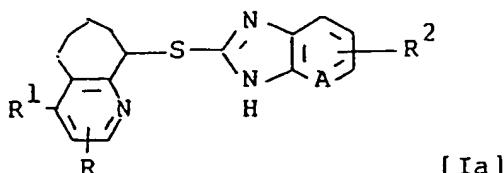


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[dans laquelle R² représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle inférieur contenant facultativement un atome d'halogène, un groupe alcoxy inférieur contenant facultativement un atome d'halogène, un groupe hydroxyle, un groupe acyle, un groupe alcoxycarbonyle inférieur, un groupe nitro ou un groupe amino ; et A représente un atome de carbone de méthine ou un atome d'azote], à faire réagir le dérivé de cyclohepténopyridine résultant représenté par la formule générale :

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(dans laquelle R, R¹, R² et A sont tels que définis ci-dessus) avec un halogénure choisi parmi les halogénures d'alkyle inférieur, les halogénures d'alcozyméthyle inférieur, les halogénures d'alkylcarbonyle inférieur, les halogénures d'alcoxycarbonyle inférieur, les halogénures d'alkylcarbonylméthyle inférieur, les halogénures d'alcoxycarbonylméthyle inférieur et les halogénures d'alkylsulfonyle inférieur, puis, facultativement, à soumettre le composé résultant à une réaction d'oxydation.

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4. Agent antiulcèreux comprenant un dérivé de cyclohepténopyridine de la revendication 1 ou un sel de celui-ci comme ingrédient actif.

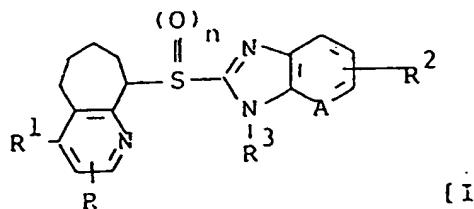
Revendications pour l'Etat contractant suivant : ES

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1. Procédé de préparation d'un dérivé de cyclohepténopyridine représenté par la formule générale :

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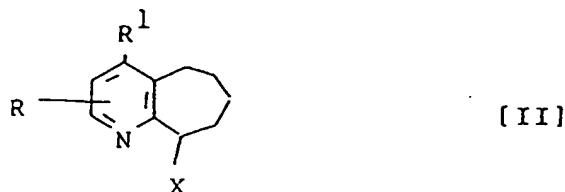
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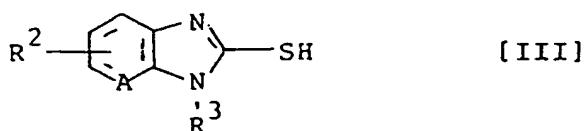
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[dans laquelle R représente un atome d'hydrogène ou un groupe alkyle inférieur ; R¹ représente un atome d'hydrogène, un atome d'halogène, un groupe alcoxy inférieur, un groupe cycloalcoxy inférieur, un groupe amido, un groupe phénoxy substitué, un groupe benzyloxy substitué, un groupe alcoxy inférieur contenant facultativement un ou plusieurs atomes d'halogène, un groupe nitro, un groupe hydroxyle, un groupe alcényloxy inférieur, un groupe alkylthio inférieur ou un groupe -NR⁴R⁵ (où R⁴ et R⁵ peuvent être identiques ou différents et représentent chacun un atome d'hydrogène ou un groupe

alkyle inférieur, ou bien R⁴ et R⁵ sont pris ensemble avec l'atome d'azote qui leur est adjacent pour former un cycle penta- ou hexagonal) ; R² représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle inférieur contenant facultativement un atome d'halogène, un groupe alcoxy inférieur contenant facultativement un atome d'halogène, un groupe hydroxyle, un groupe acyle, un groupe alcoxycarbonyle inférieur, un groupe nitro ou un groupe amino ; R³ représente un groupe alkyle inférieur, un groupe alcoxyméthyle inférieur, un groupe alkylcarbonyle inférieur, un groupe alcoxycarbonyle inférieur, un groupe carbamoyle, un groupe alkylcarbamoyle inférieur, un groupe alkylcarbonylméthyle inférieur, un groupe alcoxycarbonylméthyle inférieur, un groupe acyloxyméthyle inférieur, un groupe alkylsulfonyle inférieur, ou un groupe protecteur physiologiquement acceptable pouvant être éliminé en milieu acide ou dans des conditions physiologiques ; n représente 0 ou 1 ; et A représente un atome de carbone de méthine ou un atome d'azote] ou d'un sel de celui-ci, qui consiste à faire réagir un composé représenté par la formule générale :



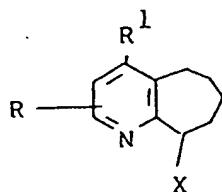
[dans laquelle R représente un atome d'hydrogène ou un groupe alkyle inférieur ; R¹ représente un atome d'hydrogène, un atome d'halogène, un groupe alcoxy inférieur, un groupe cycloalcoxy inférieur, un groupe amido, un groupe phén oxy substitué, un groupe benzyloxy substitué, un groupe alcoxy inférieur contenant facultativement un ou plusieurs atomes d'halogène, un groupe nitro, un groupe hydroxyle, un groupe alcényloxy inférieur, un groupe alkylthio inférieur ou un groupe -NR⁴R⁵ (où R⁴ et R⁵ peuvent être identiques ou différents et représentent chacun un atome d'hydrogène ou un groupe alkyle inférieur, ou bien R⁴ et R⁵ sont pris ensemble avec l'atome d'azote qui leur est adjacent pour former un cycle penta- ou hexagonal) ; et X représente un atome d'hydrogène, un atome d'halogène ou un groupe alkylsulfonyle ou arylsulfonyle] avec un composé représenté par la formule :



40 [dans laquelle R² représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle inférieur contenant facultativement un atome d'halogène, un groupe alcoxy inférieur contenant facultativement un atome d'halogène, un groupe hydroxyle, un groupe acyle, un groupe alcoxycarbonyle inférieur, un groupe nitro ou un groupe amino ; R³ représente un groupe alkyle inférieur, un groupe alcoxyméthyle inférieur, un groupe alkylcarbonyle inférieur, un groupe alcoxycarbonyle inférieur, un groupe carbamoyle, un groupe alkylcarbamoyle inférieur, un groupe alkylcarbonylméthyle inférieur, un groupe alcoxycarbonylméthyle inférieur, un groupe acyloxyméthyle inférieur, un groupe alkylsulfonyle inférieur, ou un groupe protecteur physiologiquement acceptable pouvant être éliminé en milieu acide ou dans des conditions physiologiques ; et A représente un atome de carbone de méthine ou un atome d'azote], puis à soumettre facultativement le composé résultant à une réaction d'oxydation.

- 45
- 50 2. Procédé de préparation d'un dérivé de cyclohepténopyridine de la revendication 1 ou d'un sel de celui-ci, qui consiste à faire réagir un composé représenté par la formule générale :

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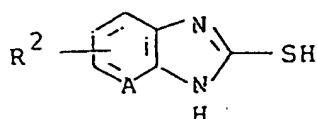


[II]

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[dans laquelle R représente un atome d'hydrogène ou un groupe alkyle inférieur ; R¹ représente un atome d'hydrogène, un atome d'halogène, un groupe alcoxy inférieur, un groupe cycloalcoxy inférieur, un groupe amido, un groupe phénoxy substitué, un groupe benzyloxy substitué, un groupe alkoxy inférieur contenant facultativement un ou plusieurs atomes d'halogène, un groupe nitro, un groupe hydroxyle, un groupe alcényloxy inférieur, un groupe alkylthio inférieur ou un groupe -NR⁴R⁵ (où R⁴ et R⁵ peuvent être identiques ou différents et représentent chacun un atome d'hydrogène ou un groupe alkyle inférieur, ou bien R⁴ et R⁵ sont pris ensemble avec l'atome d'azote qui leur est adjacent pour former un cycle penta- ou hexagonal) ; et X représente un atome d'hydrogène, un atome d'halogène ou un groupe alkylsulfonyle ou arylsulfonyle] avec un composé représenté par la formule :

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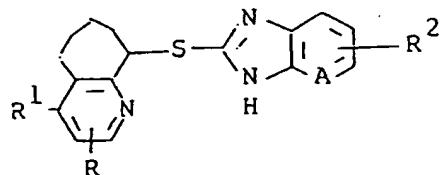
[IIIa]

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[dans laquelle R² représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle inférieur contenant facultativement un atome d'halogène, un groupe alcoxy inférieur contenant facultativement un atome d'halogène, un groupe hydroxyle, un groupe acyle, un groupe alcoxycarbonyle inférieur, un groupe nitro ou un groupe amino ; et A représente un atome de carbone de méthine ou un atome d'azote], à faire réagir le dérivé de cycloheptenopyridine résultant représenté par la formule générale :

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[Ia]

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(dans laquelle R, R¹, R² et A sont tels que définis ci-dessus) avec un halogénure choisi parmi les halogénures d'alkyle inférieur, les halogénures d'alcooxyméthyle inférieur, les halogénures d'alkylcarbonyle inférieur, les halogénures d'alcoxycarbonyle inférieur, les halogénures d'alkylcarbonylméthyle inférieur, les halogénures d'alcooxycarbonylméthyle inférieur et les halogénures d'alkylsulfonyle inférieur, puis, facultativement, à soumettre le composé résultant à une réaction d'oxydation.

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3. Procédé de préparation d'un agent antiulcèreux, consistant à mélanger un dérivé de cycloheptenopyridine préparé selon la revendication 1 ou un sel de celui-ci, comme ingrédient actif, et un support et/ou diluant.

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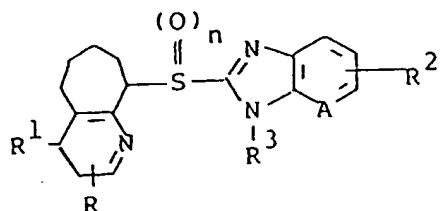
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Revendications pour l'Etat contractant suivant : GR

1. Dérivé de cyclohepténopyridine représenté par la formule générale :

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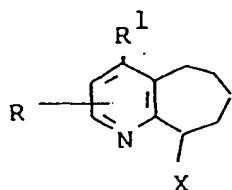
[I]

[dans laquelle R représente un atome d'hydrogène ou un groupe alkyle inférieur ; R¹ représente un atome d'hydrogène, un atome d'halogène, un groupe alcoxy inférieur, un groupe cycloalcoxy inférieur, un groupe amido, un groupe phénoxy substitué, un groupe benzyloxy substitué, un groupe alcoxy inférieur contenant facultativement un ou plusieurs atomes d'halogène, un groupe nitro, un groupe hydroxyle, un groupe alcényloxy inférieur, un groupe alkylthio inférieur ou un groupe -NR⁴R⁵ (ou R⁴ et R⁵ peuvent être identiques ou différents et représentent chacun un atome d'hydrogène ou un groupe alkyle inférieur, ou bien R⁴ et R⁵ sont pris ensemble avec l'atome d'azote qui leur est adjacent pour former un cycle penta- ou hexagonal) ; R² représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle inférieur contenant facultativement un atome d'halogène, un groupe alcoxy inférieur contenant facultativement un atome d'halogène, un groupe hydroxyle, un groupe acyle, un groupe alcoxycarbonyle inférieur, un groupe nitro ou un groupe amino ; R³ représente un groupe alkyle inférieur, un groupe alcooxyméthyle inférieur, un groupe alkylcarbonyle inférieur, un groupe alcoxycarbonyle inférieur, un groupe carbamoyle, un groupe alkylcarbamoyle inférieur, un groupe alkylcarbonylméthyle inférieur, un groupe alcoxacyarbonylméthyle inférieur, un groupe acyloxyméthyle inférieur, un groupe alkylsulfonyle inférieur, ou un groupe protecteur physiologiquement acceptable pouvant être éliminé en milieu acide ou dans des conditions physiologiques ; n représente 0 ou 1 ; et A représente un atome de carbone de méthine ou un atome d'azote] ou un sel de celui-ci.

2. Procédé de préparation d'un dérivé de cyclohepténopyridine de la revendication 1 ou d'un sel de celui-ci, qui consiste à faire réagir un composé représenté par la formule générale :

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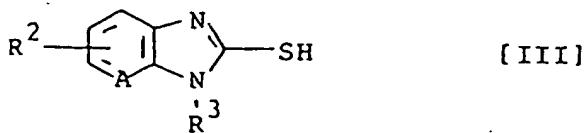
[II]

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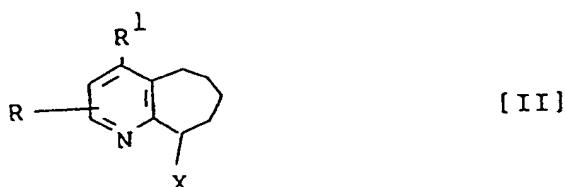
[dans laquelle R représente un atome d'hydrogène ou un groupe alkyle inférieur ; R¹ représente un atome d'hydrogène, un atome d'halogène, un groupe alcoxy inférieur, un groupe cycloalcoxy inférieur, un groupe amido, un groupe phénoxy substitué, un groupe benzyloxy substitué, un groupe alcoxy inférieur contenant facultativement un ou plusieurs atomes d'halogène, un groupe nitro, un groupe hydroxyle, un groupe alcényloxy inférieur, un groupe alkylthio inférieur ou un groupe -NR⁴R⁵ (où R⁴ et R⁵ peuvent être identiques ou différents et représentent chacun un atome d'hydrogène ou un groupe alkyle inférieur, ou bien R⁴ et R⁵ sont pris ensemble avec l'atome d'azote qui leur est adjacent pour former un cycle penta- ou hexagonal) ; et X représente un atome d'hydrogène, un atome d'halogène ou un groupe alkylsulfonyle ou arylsulfonyle] avec un composé représenté par la formule :

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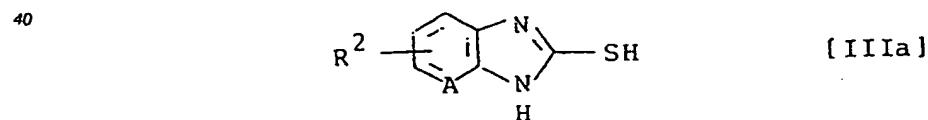


[dans laquelle R² représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle inférieur contenant facultativement un atome d'halogène, un groupe alcoxy inférieur contenant facultativement un atome d'halogène, un groupe hydroxyle, un groupe acyle, un groupe alcoxycarbonyle inférieur, un groupe nitro ou un groupe amino ; R³ représente un groupe alkyle inférieur, un groupe alcoxyméthyle inférieur, un groupe alkylcarbonyle inférieur, un groupe alcoxycarbonyle inférieur, un groupe carbamoyle, un groupe alkylcarbamoyle inférieur, un groupe alkylcarbonylméthyle inférieur, un groupe alcoxycarbonylméthyle inférieur, un groupe acyloxyméthyle inférieur, un groupe alkylsulfonyle inférieur, ou un groupe protecteur physiologiquement acceptable pouvant être éliminé en milieu acide ou dans des conditions physiologiques ; et A représente un atome de carbone de méthine ou un atome d'azote], puis à soumettre facultativement le composé résultant à une réaction d'oxydation.

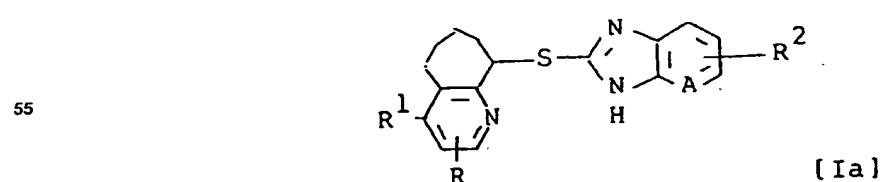
- 10 3. Procédé de préparation d'un dérivé de cyclohepténopyridine de la revendication 1 ou d'un sel de celui-ci, qui consiste à faire réagir un composé représenté par la formule générale :



30 [dans laquelle R représente un atome d'hydrogène ou un groupe alkyle inférieur ; R¹ représente un atome d'hydrogène, un atome d'halogène, un groupe alcoxy inférieur, un groupe cycloalcoxy inférieur, un groupe amido, un groupe phenoxy substitué, un groupe benzyloxy substitué, un groupe alcoxy inférieur contenant facultativement un ou plusieurs atomes d'halogène, un groupe nitro, un groupe hydroxyle, un groupe alcényloxy inférieur, un groupe alkylthio inférieur ou un groupe -NR⁴R⁵ (où R⁴ et R⁵ peuvent être identiques ou différents et représentent chacun un atome d'hydrogène ou un groupe alkyle inférieur, ou bien R⁴ et R⁵ sont pris ensemble avec l'atome d'azote qui leur est adjacent pour former un cycle penta- ou hexagonal) ; et X représente un atome d'hydrogène, un atome d'halogène ou un groupe alkylsulfonyle ou arylsulfonyle] avec un composé représenté par la formule :



45 [dans laquelle R² représente un atome d'hydrogène, un atome d'halogène, un groupe alkyle inférieur contenant facultativement un atome d'halogène, un groupe alcoxy inférieur contenant facultativement un atome d'halogène, un groupe hydroxyle, un groupe acyle, un groupe alcoxycarbonyle inférieur, un groupe nitro ou un groupe amino ; et A représente un atome de carbone de méthine ou un atome d'azote], à faire réagir le dérivé de cyclohepténopyridine résultant représenté par la formule générale :



(dans laquelle R, R¹, R² et A sont tels que définis ci-dessus) avec un halogénure choisi parmi les halogénures d'alkyle inférieur, les halogénures d'alcoxyméthyle inférieur, les halogénures d'alkylcarbonyle inférieur, les halogénures d'alcoxycarbonyle inférieur, les halogénures d'alkylcarbonylméthyle inférieur, les halogénures d'alcoxycarbonylméthyle inférieur et les halogénures d'alkylsulfone inférieur,
5 puis, facultativement, à soumettre le composé résultant à une réaction d'oxydation.

4. Agent comprenant un dérivé de cyclohepténopyridine de la revendication 1 ou un sel de celui-ci comme ingrédient actif.

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